# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS


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# INTRODUCTION TO THE SERIES

THE publication of this series of pamphlets has been undertaken to make available in a permanent form complete detailed directions for the preparation of various organic chemical reagents. In announcing this purpose it may be well to mention at the outset some of the difficulties in the way of the research chemist, which it is hoped this series will be able to overcome. The cost of chemicals is prohibitive to the majority of chemists; this was true before the war when Kahlbaum's complete supply was available, and to-day with our dependence on domestic stocks, this cost has increased. The delay in obtaining chemicals, especially from abroad, even if the expense need not be considered, is an important factor. These difficulties have therefore thrown the research chemist on his own resources. The preparation of materials for research, always time consuming and annoying, is made increasingly so by the inexactness of the published information which so often omits essential details. Because of this, much needless experimentation is necessary in order to obtain the results given in the published reports. As the additional information thus acquired is seldom published, duplication of such experiments occurs again and again,—a waste of time and material. It is hoped these difficulties may be remedied by the publication of this series of pamphlets. In other words, the authors hope to make this a clearing house for the exchange of information as to methods of preparation of some of the most needed organic chemical reagents.

On account of the impossibility of obtaining the less common organic chemicals in the United States during the past few years,

university laboratories have had no option but to prepare their own supplies. At the University of Illinois, for instance, a special study has been made of this field, and methods for the production of various substances have been investigated. As a result, reliable methods and directions have been developed for producing the materials in one-half to five pound lots. Such work as Illinois has done is now being given an even more extensive scope at the Research Laboratory of the Eastman Kodak Company. It is felt that the results from these various laboratories should be available to all chemists and it is hoped that they eventually will be completely incorporated in these pamphlets.

The organic chemicals herein discussed have been quite arbitrarily chosen, being those which have been needed in various research laboratories in the last years and for which the directions happen now to be ready for publication. The methods are in only a few cases new ones; they are in general the most satisfactory to be found in the literature. Only such details have been added as will enable a man with a reasonable amount of experience in organic chemistry to duplicate the results without difficulty. To be absolutely sure that each set of directions can be repeated, every experiment has been carried out in at least two laboratories. Only after exact duplication of the results in both laboratories are the directions considered ready for publication. The names of the chemists who have studied the various experiments are given so that further information concerning any obscure point can be obtained if any question arises in using these directions. And finally, in describing the experiments, special attention has been given to the explanation of why it is necessary to follow the directions carefully, and what will happen if these directions are not followed.

Although the main object in this series is to give the most convenient laboratory methods for preparing various substances in one-half to five pound lots, an attempt has also been made to have these processes as far as possible adaptable to large scale development. For example, extractions have been avoided wherever possible, cheap solvents have been sub-

stituted for expensive ones, and mechanical agitation, a procedure extremely important in the success of many commercial processes, has usually been specified. The apparatus used is always carefully described and wherever necessary an illustration is given. Accompanying each preparation there will be found a bibliography containing references to all the methods for the production of the substance described in the literature up to January, 1921. This is given in order to aid any future investigator who may wish to study or to improve the methods of preparation. It is not claimed that the methods are, in every case, completely perfect, but only that the yields are very satisfactory and allow the production of the substances at a reasonable cost. It is hoped therefore that the pamphlets will benefit not only the scientific research man of the university, but also the technical chemist who desires to develop the preparation of one of these substances to a large scale process of manufacture. The editors trust also that this work may be used to advantage as a preparation manual in intermediate or advanced courses in organic chemistry in university laboratories, and that it will aid small colleges in the production of necessary reagents which they are often financially unable to purchase.

The pamphlets are to be edited by the following committee: Roger Adams, University of Illinois, Urbana, Illinois; J. B. Conant, Harvard University, Cambridge, Massachusetts; H. T. Clarke, Eastman Kodak Company, Rochester, New York; Oliver Kamm, Parke, Davis Company, Detroit, Michigan; each to act for one year as editor-in-chief and the other three to assist him as associate editors. A new number of the series will appear annually, and every five years the data will be rearranged, revised, corrected, and then published in book form. The number of preparations to be completed yearly is not fixed. There will be, it is certain, about twenty; and it is hoped, as the interest is stimulated in this work, that this number may increase considerably. The editors especially desire to solicit contributions from other chemists, not only in this country but abroad. Whenever a compound is thoroughly and extensively studied in connection with some research, it is hoped that

complete directions for its preparation will be assembled and sent to the editor. He will then have them checked and published in a subsequent number. Directions for the preparation of substances already on the market are needed to make this work complete and will be gladly accepted.

It will, of course, be recognized that an occasional mistake or omission will inevitably be found in such a pamphlet as this which contains so many references and formulæ. The committee on publication will therefore deem it a favor if they are notified when any such error is discovered. It is hoped also that if any chemist knows a better method for the preparation of any of the compounds considered, or if anyone discovers any improvements in the methods, he will furnish the authors with such information. Any points which may arise in regard to the various preparations will be gladly discussed. In conclusion, the editors are ready to do all they can to make this work successful, and welcome suggestions of any kind. They feel that the success of the series will undoubtedly depend upon the cooperation of others, and as its success promises to be important to research chemists, the editors urge all interested to assist.

THE EDITORS

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# ORGANIC SYNTHESES

## I

### ALKYL AND ALKYLENE BROMIDES

$$ROH + HBr \rightarrow RBr + H_2O$$

$$ROSO_2OH + HBr \rightarrow RBr + H_2SO_4$$

Prepared by OLIVER KAMM and C. S. MARVEL.
Checked by H. T. CLARKE and ANNE W. DAVIS.

#### 1. General Procedure

A GIVEN alcohol is treated with 25 per cent excess of aqueous (48 per cent) hydrobromic acid together with sulfuric acid. The mixture is refluxed in order to convert the alcohol as completely as possible into the corresponding bromide, and the latter is then removed from the reaction mixture by distillation. Slight variations from this procedure depend upon the physical and chemical properties of the alcohol used, or of the bromide formed in the reaction. For example, in the preparations of ethyl and allyl bromides, the reaction mixture is not refluxed because of the volatility of the former compound, and because of the chemical reactivity of the latter; in the preparation of *iso*-amyl bromide, too large a proportion of sulfuric acid may produce appreciable decomposition; while halides of high molecular weight, because of their low volatility, are separated from the reaction mixture mechanically, instead of by distillation.

The use of a modified sodium bromide-sulfuric acid method for the preparation of alkyl bromides is described in connection with the preparation of *n*-butyl bromide. This method has been used also for the preparations of *iso*-amyl and trimethylene bromides, but, in general, the yields were found to be somewhat lower than those obtained with the hydrobromic-sulfuric acid method.

### (A) Hydrobromic Acid

Hydrobromic acid may be prepared conveniently by the interaction of bromine and sulfur dioxide in the presence of water.[1]

In a 3-l. round-bottom flask are placed 1200 g. of bromine, 500 cc. of water, and 1500 g. of crushed ice. A fairly rapid stream of sulfur dioxide is allowed to pass from a pressure tank into the flask, the outlet of the gas-tube being placed below the surface of the bromine layer. The flow of sulfur dioxide is adjusted at such a rate that the gas is completely absorbed. About two hours will serve for the completion of the reduction, at which time the mixture will assume a yellow color which is not removed by further addition of sulfur dioxide, an excess of which is to be avoided. To prevent loss of gaseous hydrobromic acid, it is advisable to cool the mixture during the progress of the reduction. It is advisable also to agitate the mixture occasionally during the first stage of the reduction.

When the reduction is completed, the flask is connected with a condenser and the mixture subjected to distillation. The boiling point of constant boiling hydrobromic acid is 125–126° at 760 mm., but it must be remembered that in distilling the product from the sulfuric acid mixture, the thermometer reading should not be relied upon as an index to the composition of the distillate. Towards the end of the distillation the thermometer may rise to 130° and above, when water with only traces of acid distils from the sulfuric acid residue. Upon redistillation of the product the thermometer reading may be relied upon. For many uses a product free from traces of

[1] J. Chem. Soc. 77, 648 (1900). Pickles recommends preparing hydrobromic acid from potassium bromide and sulfuric acid in the presence of a little stannous salt to prevent the formation of traces of bromine. Chem. News, 119, 89 (1919).

sulfuric acid is not required and one distillation is sufficient. In such cases the progress of the distillation is followed by determinations of the specific gravity of the distillate.

According to the above procedure, 20 kg. of 48 per cent hydrobromic acid were prepared from 10.3 kg. of bromine. The actual time required by one man for the preparation of this quantity was twenty-three hours.

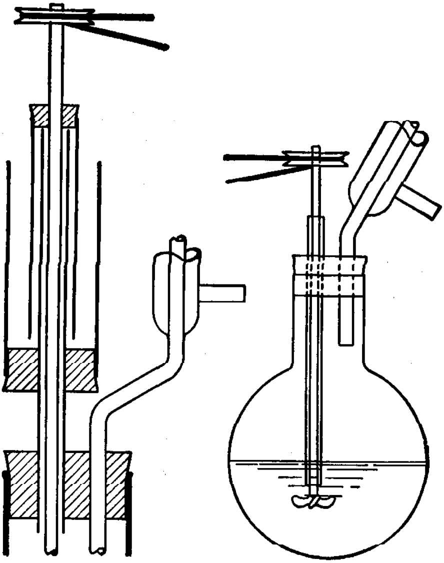
For the preparation of alkyl bromides on a relatively large scale the hydrobromic acid need not be distilled but may be used directly for the subsequent preparation. The fact that 0.5 mole of sulfuric acid is present for each mole of hydrobromic acid is not a disadvantage, since the presence of sulfuric acid is desired, and consequently a correspondingly smaller quantity need be added.

## (B) Allyl Bromide

In a 3-l. round-bottom flask, a hydrobromic acid solution is made by the sulfur dioxide reduction of 480 g. of bromine in the presence of 510 g. of ice water or a mixture is made of 1000 g. of aqueous 48 per cent hydrobromic acid and 300 g. of concentrated sulfuric acid. To this are added 385 cc. of aqueous allyl alcohol, which, according to bromine titration, contain 233 g. of pure allyl alcohol. The 3-l. round-bottom flask is fitted with a mechanical stirrer (Fig. 1, p. 4, see also Notes), separatory funnel, and an efficient condenser set for downward distillation. Stirring is started and 300 g. of concentrated sulfuric acid are added gradually through the separatory funnel to the warm solution. The allyl bromide distils over completely in about one-half to one hour. The crude allyl bromide is washed with dilute sodium carbonate solution, is dried over calcium chloride and is distilled. The yield of product boiling at 69–72° from a number of experiments varies from 445 to 465 g. (92–96 per cent theory). A small high-boiling fraction is also obtained and examination has shown this to consist of propylene bromide.

### (C) *iso*-Amyl Bromide

In a 5-l. round-bottom flask, a hydrobromic acid solution is prepared (details under (A) "Hydrobromic Acid") by passing sulfur dioxide into a mixture of 1100 g. of crushed ice and 1000 g. of bromine. This is equivalent to a mixture of 2100 g.



(*a*) (*b*)

Fig. 1.

of 48 per cent hydrobromic acid and 600 g. of concentrated sulfuric acid. There are then added 880 g. of *iso*-amyl alcohol (b. p. 130–132°) and 100 g. of concentrated sulfuric acid in the order mentioned. The clear homogeneous solution is refluxed gently during a period of three hours. Even during the early stages of the heating, the separation of *iso*-amyl bromide is observed and the reaction appears to be complete after about

one hour. The product is isolated as in the preparation of *n*-butyl bromide.

A yield of 1435 g. of crude product is obtained. After purification with concentrated sulfuric acid the product weighs 1410 g. (93 per cent theory). Upon fractionation, however, it is found that appreciable amounts of high-boiling product are present and therefore the yield of fractionated material boiling over the range 116–120° varies in different experiments from 1330 to 1360 g. (88–90 per cent theory).

## (D) *n*-Butyl Bromide

*Hydrobromic-sulfuric Acid Method.* In a 5-l. round-bottom flask are placed 1300 g. of crushed ice and 1200 g. of bromine. The flask is cooled in an ice water bath and sulfur dioxide is passed into the mixture until the red color due to free bromine has just disappeared (details under (A) "Hydrobromic Acid"). This mixture is equivalent to 2500 g. of 48 per cent hydrobromic acid to which 750 g. of concentrated sulfuric acid have been added.

888 g. of *n*-butyl alcohol are added to the sulfuric-hydrobromic acid mixture. Following this, 600 g. of concentrated sulfuric acid are added in several portions, with shaking. The flask is then attached to a reflux condenser and the mixture is refluxed during a period of three hours, during which time the formation of butyl bromide is carried practically to completion. The flask is now fitted with a condenser set downward and the product removed from the reaction mixture by direct distillation (about one hour). The water-insoluble layer is separated, washed first with water, then with 200 g. of cold concentrated sulfuric acid, and finally with a sodium carbonate solution (50 g. of sodium carbonate in 500 cc. of water). The product is separated as completely as possible from the aqueous layer, dried during several hours with a small quantity (15 to 25 g.) of calcium chloride, and distilled. The yield of product boiling between 101–104° is 1560 g. (95 per cent theory).

*Sodium Bromide Method.* In a 5-l. round-bottom flask are placed 1350 cc. of water and then with stirring 1545 g. (15 moles) of finely powdered sodium bromide are added. It is advisable to add the salt to the water in this manner in place of the reverse procedure, in order to avoid caking of the sodium bromide. 888 g. (12 moles) of *n*-butyl alcohol and then gradually 2000 g. of concentrated sulfuric acid are added. The last half of the acid is added through a dropping funnel after the flask has been connected with a reflux condenser. The mixture is shaken occasionally during the addition of the sulfuric acid because of a tendency to separate into layers, and is finally refluxed during a period of four hours. The condenser is then set downward and the butyl bromide removed by distillation. The product is purified as in the preceding experiment, the yield of product boiling between 101–104° being 1480 g. (90 per cent theory).

## (E) Ethyl Bromide

In the preparation of hydrobromic acid for the manufacture of ethyl bromide, particular care must be taken to avoid the presence of any excess of sulfur dioxide gas. The evolution of gas during the distillation of the ethyl bromide will invariably result in a large loss of this volatile product (b. p. 38–39°).

A hydrobromic acid solution is prepared in a 5-l. round-bottom flask by the reduction of 1000 g. of bromine in the presence of 1100 g. of cracked ice. Experimental details have been given under (A) "Hydrobromic Acid." A mixture of 2075 g. of aqueous (48 per cent) hydrobromic acid and 600 g. of concentrated sulfuric acid may be used in place of the above reduction mixture. After the addition of 500 g. of ordinary 92 per cent ethyl alcohol, the flask is attached to a long condenser set ready for distillation and 1000 g. of concentrated sulfuric acid are slowly added through a separatory funnel. Because of the volatility of ethyl bromide, the mixture is not heated under reflux, but is subjected instead to slow distillation. The end of the condenser is provided with an adapter tube, and the distillate is collected in a flask containing ice water. The crude

ethyl bromide, weighing 1055 g., is purified as directed under the butyl bromide experiment. The washing with concentrated sulfuric acid is almost superfluous unless a product of special purity is desired; for instance, in the present experiment a washing with 300 g. of concentrated acid results in a decrease in weight of only 10 g.

The product is washed and purified as in the butyl bromide preparation. It is distilled from a water bath and boils at 38.5–39.5°, provided chips of porous plate are added to prevent superheating. Final yields vary from 90–95 per cent of the theory according to the precautions taken to prevent losses due to evaporation.

### (F) Lauryl Bromide

In a 250 cc. round-bottom flask are placed 70 g. of hydrobromic acid (48 per cent) and 22 g. of concentrated sulfuric acid. To this mixture are added 40 g. of lauryl alcohol (b. p. 188–192° at 110 mm.) and the mixture is then refluxed for five hours. The bromide is isolated as described in the preparation of octyl bromide. The product is distilled under reduced pressure and is collected from 175–180° at 45 mm. The yield is 49 g. (91 per cent theory).

### (G) *n*-Octyl Bromide

In a 500 cc. round-bottom flask are placed 240 g. of hydrobromic acid (48 per cent), 62 g. of concentrated sulfuric acid, and 71 g. of *n*-octyl alcohol (b. p. 135–140° at 100 mm.). The mixture is boiled under reflux for three and a half hours. The solution is diluted with water and the bromide layer is separated, washed once with a little cold concentrated sulfuric acid, then with water and finally with dilute sodium carbonate solution. The crude yield is 102 g.; this is dried over a little calcium chloride and distilled. The product is collected at 196–200° and amounts to 96 g. (91 per cent theory).

### (H) Trimethylene Bromide

In a 5-l. round-bottom flask are placed 1200 g. of bromine and 1300 g. of crushed ice. The bromine is reduced with sulfur dioxide as already directed under (A) "Hydrobromic Acid." In place of the above reduction mixture, there may be used a mixture of 2500 g. of aqueous 48 per cent hydrobromic acid and 750 g. of concentrated sulfuric acid.

456 g. of trimethylene glycol (b. p. 210–215°) and 1200 g. of concentrated sulfuric acid are next added in the order given, the sulfuric acid being added slowly. The mixture is refluxed during a period of three hours and is then subjected to distillation until no water-insoluble product appears in the distillate (about one hour).

The trimethylene bromide is purified as directed under "*n*-Butyl Bromide." A yield of 1088 g. boiling at 162–165° (90 per cent theory) is obtained. In a number of experiments, the lowest yield obtained was 88 per cent, whereas the maximum obtained was 95 per cent.

*Sodium Bromide Method.* The yields of trimethylene bromide by the sodium bromide method as described under "*n*-Butyl Bromide" are slightly lower than those given above. Thus, from 1350 g. of water, 1545 g. of sodium bromide, 456 g. of trimethylene glycol, and 2500 g. of sulfuric acid, a yield of 1110 g. of crude product is obtained, from which, after purification and distillation, a yield of 1030 g. of bromide (85 per cent theory) is obtained.

## 2. Notes

*Hydrobromic Acid.* In the sulfur-dioxide reduction of bromine, it should be noted that the proportion of water used depends upon whether the reduction mixture is to be distilled for the preparation of 48 per cent hydrobromic acid, or whether it is to be used directly for the manufacture of alkyl bromides.

During the first stage of the reduction, the flask should be shaken from time to time in order to avoid the accumulation of

sulfur dioxide, or possibly of sulfuryl bromide, which would result in a violent reaction due to a large quantity of the material reacting at one time. Although more than a hundred reduction experiments were conducted with quantities of bromine varying from 0.5 to 2 kg., this sudden reaction was noted in only one or two instances in spite of the fact that there was usually no agitation other than that furnished by the entering gas stream.

The intensity of the color in the reduced bromine solution depends somewhat on the quality of bromine used, and with the technical product special care is needed in noting the end-point of the reduction; i.e., the transition from the bromine color to a yellowish-brown color.

An excess of sulfur dioxide is to be avoided for the reason that evolution of gas during the distillation of the product will result in a considerable loss of alkyl bromide through volatilization. This loss is especially marked in the preparations of ethyl and allyl bromides if this precaution is not observed.

*Alkyl Bromides; General Discussion.* When an alcohol is heated with aqueous 48 per cent hydrobromic acid, a partial conversion takes place into the corresponding bromide. The reaction is, however, more rapid and more complete in the presence of sulfuric acid. Although the constant boiling hydrobromic acid obtainable on the market may be used in all the above experiments, its preparation by the sulfur-dioxide reduction of bromine will be considerably cheaper and equally convenient, provided a cylinder of sulfur dioxide is available. For use in the preparation of alkyl bromides, distillation of the bromine-sulfur dioxide reduction mixture is superfluous.

The method described is quite general for the preparation of primary bromides. The presence of sulfuric acid would usually be objectionable in the preparation of secondary and tertiary bromides because of the ease of dehydration of the corresponding alcohols. Moreover, these bromides may be obtained in good yields without the use of sulfuric acid.

The reaction mixture is heated under the reflux condenser for several hours preliminary to the first distillation of the alkyl

bromide. This is done in order to convert the alcohol as completely as possible into the corresponding bromide and thus to prevent its volatilization with the bromide. Direct distillation of the reaction mixture without refluxing will usually result in a decrease in yield of from 5–15 per cent. Alkyl bromides of low molecular weight may, however, be distilled directly from the reaction mixture without the necessity of refluxing, providing that the process of distillation is conducted very slowly. Alkyl halides of high molecular weight are separated from the reaction liquors mechanically instead of by distillation. This is done in order to avoid the decomposition due to heating the slightly volatile material with a gradually increasing concentration of sulfuric acid.

The favorable results obtained in the preparation of alkyl bromides with aqueous hydrobromic acid to which sulfuric acid has been added suggests that practically the same result might be accomplished by the use of sodium bromide, water, and sulfuric acid in such ratios as approximate the proportions used in the first instance. In actual practice this modified sodium bromide method was found fairly satisfactory for the preparation of butyl bromide and of trimethylene bromide. Slightly lower yields are due to the decreased solubilities of the alcohols in the reaction mixtures because of the presence of dissolved salts. One would therefore predict that with alcohols of still higher molecular weights, even lower yields would be obtained with the sodium bromide method. This prediction was substantiated in experiments with *iso*-amyl alcohol, where the sodium bromide method gave yields of only 70 per cent of the theory, whereas the hydrobromic acid method gave yields of almost 90 per cent. The sodium bromide method is therefore not recommended for the preparation of alkyl bromides of high molecular weight.

The main impurities usually found in alkyl halides are the corresponding alcohols and ethers. Cold concentrated sulfuric acid is an efficient reagent for the removal of these impurities in all cases where the alkyl halide itself is not attacked by this reagent. Whenever a product contains a considerable quantity

of unchanged alcohol, several washings with the cold concentrated acid may be required.

Trimethylene bromide prepared by direct distillation of the reaction mixture without the preliminary refluxing period contains appreciable amounts of trimethylene bromohydrin. In the purification of trimethylene bromide with sulfuric acid the high specific gravity of the former (1.987) must be borne in mind. Vigorous shaking with sulfuric acid may result in the formation of emulsions.

In the preparation of allyl bromide, appreciable loss may occur, not only because of carbonization but primarily because of the reaction of the allyl bromide with hydrobromic acid to form propylene bromide. Stirring during the formation of the alkyl bromide prevents the formation of two layers in the reaction mixture and thus assures a rapid and smooth distillation. An efficient condenser is of course essential.

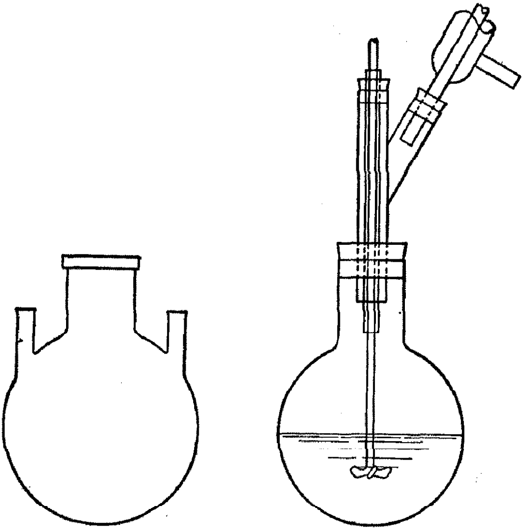
In the experiments described, a more dilute hydrobromic acid solution may be used, provided that the proportion of sulfuric acid is increased. Aqueous solutions of alcohols may also be used, provided a suitable adjustment is made of the proportion of sulfuric acid. In the allyl alcohol experiment, material was used as obtained from the glycerol formic acid preparation after one salting-out with potassium carbonate.

In many organic preparations too large a quantity of drying agent is usually employed, with the resulting loss of a considerable amount of material due to absorption by the drying agent. In the present experiments it is found that after a careful separation of the alkyl halide from the water layer as small a quantity as 15 g. of calcium chloride is sufficient for the drying of 1500 g. of alkyl halide.

Mechanical stirring is often avoided in most university laboratories and since it is so important in obtaining successful yields, it will be specified in many experiments. In Fig. 1 (p. 4) (*a*) and (*b*) represent two convenient types of stirring devices [1] where refluxing and stirring are desired at the same time. When the stopper of the flask is so small that it will hold only the

[1] Ber. **37**, 923 (1904).

mechanical stirrer, a Y-tube such as is shown in Fig. 2, (*b*) fitted with either form of stirrer is suitable. It often happens that a separatory funnel or thermometer must also be inserted in the flask in addition to the reflux condenser. A flask such as is shown in Fig. 2, (*a*) is especially convenient, the middle



(*a*) (*b*)

FIG. 2.

opening being used for the stirrer, the two smaller ones for thermometer and reflux condenser.

### 3. Other Methods of Preparation

Alkyl halides are prepared most conveniently from the corresponding alcohols. The methods commonly employed are (*a*) by the action of phosphorus bromide,[1] (*b*) by the action of a

[1] Ann. chim. phys. (2) **34**, 99 (1827); Ann. **30**, 298 (1839); **56**, 146 (1845); **98**, 114 (1855).

metallic bromide and sulfuric acid,[1] (*c*) by the action of very concentrated or fuming hydrobromic acid often under pressure,[2] and (*d*) by the action of aqueous hydrobromic acid according to the method suggested by Norris.[3]

Bodroux [4] has prepared allyl, propyl, and isobutyl bromides by means of a modified Norris method. Bromine was reduced by means of sulfur dioxide, the alcohol was added and the mixture distilled. The yields were not the highest, however. The method described above is an improvement of the Norris-Bodroux method. Two essential modifications consist in the addition of concentrated sulfuric acid, and in the recommendation of a refluxing period preliminary to the distillation. The sodium bromide method has been improved by the introduction of similar modifications.

Two papers [5] have appeared recently aiming at the improvement of the preparation of ethyl bromide. Although the preparation of allyl bromide was studied as recently as 1913, yields of only 60–85 per cent are reported by Claisen and Eisleb.[6]

For the preparation of trimethylene bromide, the most convenient laboratory method in the past has been the addition of hydrobromic acid to allyl bromide;[7] it has also been made by the action of gaseous and aqueous hydrobromic acid on glycerol.[8] Since trimethylene glycol is at the present time a by-product obtained from the purification of glycerol, a more convenient and practical method for the preparation of trimethylene bromide consists in the utilization of the corresponding glycol. A method involving the use of gaseous hydrogen bromide has recently been described,[9] but the aqueous hydrobromic-sulfuric acid method [10] is found to be a considerable improvement.

[1] J. **1857**, 441.
[2] Ann. **136**, 41 (1865); **158**, 161 (1871); **159**, 73 (1871).
[3] Am. Chem. J. **38**, 639 (1907); J. Am. Chem. Soc. **38**, 1075 (1916).
[4] Compt. rend. **160**, 206 (1915).
[5] J. Chem. Soc. **107**, 1489 (1915); **109**, 1 (1916).
[6] Ann. **401**, 27 (1913).
[7] Ann. **158**, 370 (1871); Ann. **197**, 179 (1879).
[8] Monatsh. **2**, 639 (1881).
[9] J. Am. Chem. Soc. **40**, 546 (1918).
[10] J. Am. Chem. Soc. **43**, 2228 (1922).

II

## ALLYL ALCOHOL

$$CH_2OHCHOHCH_2OH + HCO_2H \rightarrow CH_2OHCHOHCH_2OCOH \rightarrow CH_2{=}CHCH_2OH + H_2O + CO_2$$

Prepared by Oliver Kamm and C. S. Marvel.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure*

In a 5-l. round-bottom flask are placed 2 kg. of glycerol and 700 g. of technical 85 per cent formic acid. The flask is connected with a condenser set for downward distillation and the temperature within the reaction mixture is indicated by a thermometer, the bulb of which is immersed in the liquid. It is advisable to use as a receiver a boiling flask attached tightly to the lower end of the condenser. A tube is then run from the side arm of the boiling flask to a bottle of strong caustic soda to dissolve and decompose any acrolein which may be formed; a few pieces of clay plate are added to the distillation flask in order to prevent bumping, and it is then heated rapidly over a good ring burner. The first runnings should come over within fifteen minutes and a temperature of 195° should be reached within from thirty to forty-five minutes. Slow heating causes charring and formation of much acrolein, and thus gives a very low yield of allyl alcohol. The distillate collected up to the point where the thermometer registers 195° is saved separately. The heating of the reaction mixture is continued until the temperature reaches 260°, the main reaction taking place at from 225° to 235°. At this point, when the heating should be stopped, a white smoke appears and decomposition apparently begins. The distillate (about 750 cc.) coming over between the ther-

* See Org. Syn. 6, 103, for additional information concerning the preparation of allyl alcohol.

mometer readings of from 195–260° is saved. For this operation about four hours are required. The contents of the flask are now allowed to cool to a temperature between 100° and 125° and 500 g. more of the technical 85 per cent formic acid are added. The distillation is then repeated in exactly the same manner as described above and 500 cc. of distillate are collected between the temperatures from 195–260°. The reaction mixture is allowed to cool again and a third portion of 500 g. of formic acid is added. This distillation yields not more than 350 cc. of the desired fraction, and this low yield indicates that the glycerol is used up and that further addition of formic acid is unnecessary; moreover, the residue left behind is now small, amounting only to 100 to 200 cc. The three distillations require from one to one and a half days.

The 195–260° fractions of the distillates are treated with potassium carbonate to salt out the allyl alcohol and to neutralize the little formic acid present. This allyl alcohol is then distilled and the fraction boiling up to about 103° is collected, or if a column is used, up to 98°. In this way, 845 g. of an allyl alcohol are obtained, which by a bromine titration shows a purity of about 68–70 per cent. This is equivalent to 570 to 590 g. of pure allyl alcohol (45–47 per cent theory).

The alcohol may be made practically anhydrous by refluxing with successive portions of fused potassium carbonate until no further action is observed. The carbonate will remain finely divided and will not become sticky when water is absent. A considerable amount of allyl alcohol is lost mechanically during the drying in this way, so that the potassium carbonate which is used here should be employed for the salting out of fresh portions of allyl alcohol in the first part of subsequent preparations. The allyl alcohol thus produced is dry enough for all practical purposes (98–99 per cent) and it is unnecessary to dry with lime or barium oxide as advised in the literature in order to remove all of the water. The allyl alcohol obtained by this process boils at 94–97°.

Clarke and Taylor have used the following method with success for obtaining a completely anhydrous product. The

allyl alcohol obtained after one salting out with potassium carbonate is distilled as indicated above to give a product of about 70 per cent purity and then mixed with 0.25 of its volume of carbon tetrachloride. The mixture is then slowly distilled from a round-bottom flask fitted with a fractionating column at least 80 cm. long, collecting the low boiling mixture of carbon tetrachloride, water, and allyl alcohol, drying it with potassium carbonate, and returning it to the flask. This process is repeated several times, until only very little water passes over. The mixture is then completely distilled, taking the following cuts: $-80°$, 80–90°, 90–95°, 95.5–97°, the last being alcohol which titrates 100 per cent pure. The lower fractions are dried separately and refractionated, thus giving an additional portion boiling 95.5–97°.

## 2. Notes

The reaction between formic acid and glycerol runs very smoothly and without the tendency toward foaming which results when oxalic acid is used.

The lower fraction which distils up to the point where the thermometer registers 195° contains a considerable amount of formic acid and in large scale production it would undoubtedly pay to recover it.

To determine the purity of any sample of allyl alcohol, 1 cc. is run into 15 to 25 cc. of carbon tetrachloride and this solution is then treated in the cold with a carbon tetrachloride solution of bromine (standardized with potassium iodide and sodium thiosulfate) until a permanent bromine coloration is obtained. The amount of allyl alcohol present in any solution may also be determined roughly by conversion to allyl bromide. From several experiments it was found that the allyl bromide obtained was equivalent to the amount of allyl alcohol as determined by bromine titration.

A large amount of work was carried out upon the oxalic acid and glycerol method for the production of allyl alcohol. The results, however, were not satisfactory and therefore are not included here. It might be said, however, that when oxalic

acid is used in place of formic acid, the reaction requires a longer time for completion and is not nearly so smooth. There is a much greater tendency toward foaming and the reaction must be continually watched in order to prevent this, especially after the first distillation with oxalic acid, when more oxalic acid is added and heating is continued. Another disadvantage is that large amounts of acrolein are produced when oxalic acid is used. In general, the yield by this method amounts to not over 20–30 per cent, whereas with formic acid a yield of 45–50 per cent is easily obtained. As far as the preparation of allyl alcohol is concerned, in amounts such as are used in the above experiments, the formic acid method is greatly to be preferred. The method of employing anhydrous oxalic acid, which has been reported as giving particularly good yields, did not give satisfactory results when tried.

Experiments were also made with 90 per cent formic acid and yields of 50–54 per cent of allyl alcohol were obtained. The importance of heating the original reaction mixture rapidly should be again emphasized.

### 3. Other Methods of Preparation

The methods for making allyl alcohol are many. It may be prepared by (*a*) the action of metals upon dichlorohydrin;[1] (*b*) the reduction of acrolein;[2] (*c*) the action of potassium hydroxide on trimethylene bromide;[3] (*d*) the catalytic decomposition of glycerol with aluminum oxide;[4] (*e*) the hydrolysis of allyl iodide;[5] (*f*) the decomposition of glycerol triformate;[6] (*g*) the action of formic acid upon glycerin;[7] and (*h*) the action of

[1] Ann. chim. phys. (3) **67**, 323 (1863); Ann. **159**, 173 (1871); Z. Chem. **4**, 259 (1868).

[2] Ann. Spl. **3**, 258 (1864); Ber. **45**, 3316 (1912).

[3] J. Russ. Phys. Chem. Soc. **45**, 568 (1913); Chem. Zentr. **1913**, II, 1374.

[4] Compt. rend. **166**, 1033 (1918).

[5] Ann. **102**, 288 (1857).

[6] Z. physik. Chem. **70**, 460 (1910).

[7] Ann. **156**, 139 (1870); Bull. soc. chim. (4) **13**, 1103 (1913); C. A. **10**, 1035 (1916).

oxalic acid upon glycerin.[1] Of these methods, the two most practical for the preparation of allyl alcohol upon a large scale are by the action upon glycerol of either formic or oxalic acid. Both have been studied, with the result that the formic acid method is shown to be much the superior.

The use of mixtures of glycerol and formic acid for the preparation of allyl derivatives (allyl chloride and allyl formate) has recently been described by Aschan.[2] Allyl alcohol has also been isolated from crude wood alcohol.[3] A special method for titrating allyl alcohol has been described.[4]

[1] Ann. chim. phys. (6) **22**, 464 (1891); Ann. **167**, 222 footnote (1873); **156**, 134, 149 (1870); J. Chem. Soc. **105**, 151 (1914); **107**, 407 (1915).

[2] C. A. **13**, 2868 (1919).

[3] Ber. **7**, 1381, 1493 (1874); Z. angew. Chem. **22**, 2037 (1909).

[4] Monatsh. **39**, 617 (1918).

# BENZENE SULFONYL CHLORIDE

(*a*) $PCl_5 + 3C_6H_5SO_2ONa \rightarrow 3C_6H_5SO_2Cl + 2NaCl + NaPO_3$
(*b*) $POCl_3 + 2C_6H_5SO_2ONa \rightarrow 2C_6H_5SO_2Cl + NaCl + NaPO_3$

Prepared by Roger Adams and C. S. Marvel.
Checked by H. T. Clarke and W. W. Hartman.

## 1. Procedure

(*a*) Phosphorus Pentachloride Method:—In a 2-l. round-bottom flask is placed a mixture of 250 g. (1.15 moles) of finely divided phosphorus pentachloride and 450 g. (2.5 moles) of sodium benzene sulfonate which has previously been dried for three hours at 140°. The mixture is heated in an oil bath at 170–180° for fifteen hours. It is advisable to have a reflux condenser attached to the flask, although very little active refluxing takes place. Every four hours during the heating period, the flask should be removed from the oil bath, cooled for fifteen minutes, stoppered and shaken thoroughly until the mass becomes pasty (sometimes ten to fifteen minutes are required to accomplish this). At the end of the heating period, the mixture is cooled and 1 l. of water with 1 kg. of cracked ice are added. Benzene sulfonyl chloride sinks to the bottom, is separated, washed once with water, filtered if necessary, and vacuum distilled for purification. The forerun, consisting of a little chlorobenzene, water, and a little benzene sulfonyl chloride is discarded and the fraction boiling between 145–150° at 45 mm. is collected. This weighs in the different runs from 330 to 360 g. (75–80 per cent theory).

The yields in this experiment are likely to vary widely on account of the variability in the different samples of sodium

benzene sulfonate. With certain samples a solid impurity is left as a residue from the distillation of the crude benzene sulfonyl chloride.

(*b*) Phosphorus Oxychloride Method:—Benzene sulfonyl chloride may be prepared by the same procedure described above from a mixture of 270 g. (3 moles) of sodium benzene sulfonate and 180 g. (2.25 moles) of phosphorus oxychloride. It is advisable to observe the same precaution about shaking every few hours. The yield of finished product boiling 145–150° at 45 mm. amounts to 195 to 230 g. (75–90 per cent theory).

## 2. Notes

It is advisable to heat the mixture just described as long as fifteen hours to be certain that the reaction is complete. The reaction is chiefly over, however, at the end of ten hours.

The temperature must be maintained at 170°. A lower temperature does not give so good a yield.

If a means of mechanical stirring were provided, the yields would undoubtedly be much better, and the time required shorter. The mixtures, however, are so thick that in the laboratory mechanical stirring is impracticable.

Experiments using a larger excess of phosphorus pentachloride or phosphorus oxychloride were used but no particular advantage was so obtained.

## 3. Other Methods of Preparation

Benzene sulfonyl chloride may be made by the action of phosphorus pentachloride upon benzene sulfonic acid or its salts;[1] by the action of phosphorus oxychloride upon the salts of benzene sulfonic acid;[2] by the action of chlorosulfonic acid upon benzene;[3] by the action of chlorosulfonic acid upon the

[1] Ann. **87**, 299 (1853); **119**, 143 footnote (1861); **275**, 233 (1893); Z. chem. **1866**, 106; Ber. **5**, 876 (1872); Rec. trav. chim. **18**, 432 (1899).

[2] Compt. rend. **35**, 690 (1852).

[3] Z. Chem. **1869**, 41; Ber. **4**, 356 (1871); **11**, 2061 (1878); **12**, 1848 (1879); **42**, 1802, 2057 (1909).

sodium salts of benzene sulfonic acid.[1] Since the sodium benzene sulfonate is a commercial product which may be obtained from the phenol manufacturers, the conversion of it into the sulfonyl chloride has been especially studied. In the laboratory manuals, the directions generally involve the action of 1 mole of phosphorus pentachloride upon 1 mole of sodium benzene sulfonate. This method requires that the large amount of phosphorus oxychloride formed be destroyed or distilled off, a process which not only requires considerable time, but which is also rather wasteful. It is much more economical, however, to treat sodium benzene sulfonate with phosphorus pentachloride in such proportions that the phosphorus oxychloride which is produced in the initial reaction will convert more sodium benzene sulfonate into benzene sulfonyl chloride. This method is, to be sure, described in the literature and it is claimed that nearly quantitative yields are obtained. It was impossible with the grade of sodium benzene sulfonate which was available to duplicate these published results. It is also possible to produce benzene sulfonyl chloride by the action of phosphorus oxychloride upon sodium benzene sulfonate and the yields in this case were about the same as when phosphorus pentachloride was used. These last two methods are better than the original one because with no phosphorus oxychloride or pentachloride to destroy, working up of the crude material is very easy.

Although it is claimed in the literature that chlorosulfonic acid and benzene give good yields of benzene sulfonyl chloride it was found that a large excess of chlorosulfonic acid was necessary; also that much greater precautions must be taken in carrying out the reaction. If very large amounts of benzene sulfonyl chloride were needed, it would probably be advisable to study this latter reaction intensively with the possibility of developing it satisfactorily.

[1] Ber. 15, 1118 (1882).

IV

# BENZIL

$$C_6H_5CHOHCOC_6H_5+O(HNO_3) \rightarrow C_6H_5COCOC_6H_5+H_2O$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by J. B. CONANT and C. E. BILLS.

## 1. Procedure*

IN a 3-l. round-bottom flask are placed 410 g. of crude benzoin and 1 l. of nitric acid (sp. gr. 1.42), (2.5 cc. of nitric acid per gram of benzoin). The mixture is heated on a water bath for about one hour with occasional shaking, until the evolution of oxides of nitrogen ceases. The reaction mixture is then poured with stirring into four to five times its volume of cold water; the benzil precipitates as small yellow lumps. The crude product is filtered and washed several times with water to remove the nitric acid. The yield after drying is 390 to 395 g. (96–97 per cent theory). Absolutely pure benzil may be obtained by crystallization from an alcohol solution. 390 g. of the crude benzil may be dissolved in about 1 l. of boiling alcohol: and since pure benzil is quite insoluble in cold alcohol, there is no difficulty in obtaining 370 g. of the pure product from the 390 g. used.

## 2. Notes

A number of experiments upon the oxidation of benzoin to benzil with nitric acid were made in which the mixture was stirred continuously. An inferior grade of product and smaller yields (seldom over 75 per cent) were obtained. The probable reason for this is to be found in the fact that benzoin is readily soluble in nitric acid while the benzil is not, and the latter there-

* See Org. Syn. 6, 6, for a second and perhaps more satisfactory method of preparing benzil.

fore floats on the top as soon as it has formed. If a stirrer is employed, it tends to bring the precipitated benzil into intimate contact with the nitric acid, causing some of it to become further oxidized or nitrated, and thus reducing the yield and quality of the product.

In E. Fischer's "Anleitung zur Darstellung Organischer Präparate" 8th edition (1908) p. 35, the following test is given to determine when all the benzoin has been oxidized. A drop of the oil is treated with water to cause it to solidify. The crystals thus produced are dissolved in alcohol, diluted with water, a little Fehling's solution is added and the mixture is heated to 60–70°. If benzoin is present, cuprous oxide is precipitated. In general, however, the test is unnecessary and the cessation of the evolution of oxides of nitrogen is a satisfactory end-point.

### 3. Other Methods of Preparation

Benzil is very readily formed by the oxidation of benzoin, with nitric acid,[1] a method first described by N. Zinin. Various other oxidizing agents[2] may be employed, but according to the literature none of these give entirely satisfactory results; they have therefore not been investigated. Other methods for preparing benzil, obviously of theoretical importance only as compared with the oxidation of benzoin, have appeared but have not been studied. Thus preparations have been carried out by the action of acetic acid and zinc[3] or of heat on benzoin;[4] by the action of boiling water on tolane dibromide[5] or stilbene dibromide;[6] by the action of sulfuric acid or acetic acid upon tolane tetrachloride;[7] by the action of cyanogen on benzene in the

[1] Ann. **34**, 188 (1840).

[2] With chlorine, Ann. **17**, 91 (1836); electrolytic oxidation, J. Am. Chem. Soc. **21**, 893 (1899).

[3] J. Chem. Soc. **71**, 219 (1897).

[4] Ber. **30**, 2923 (1897).

[5] Ber. **4**, 380 (1871).

[6] Ann. **145**, 338 (1868).

[7] Ber. **12**, 1975 (1879).

presence of aluminum chloride;[1] by the nitration of acetyl benzoin and stilbene-diol diacetates;[2] by the hydrolysis of hydrazobenzil.[3]

[1] Ber. **44**, 2457 (1911).
[2] J. Chem. Soc. **99**, 345, 348 (1911).
[3] J. prakt. Chem. (2) **83**, 217, 226, 232 (1911).

# V

## BENZILIC ACID

$$C_6H_5COCOC_6H_5 + KOH \rightarrow (C_6H_5)_2C(OH)CO_2K$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by J. B. CONANT and C. E. BILLS.

### 1. Procedure

IN a 5-l. round-bottom flask, 350 g. of potassium hydroxide are dissolved in 700 cc. of distilled water, and 700 g. of alcohol (95 per cent) and 350 g. of pure benzil are added. A deep bluish-black solution is produced. The mixture is placed on a steam bath and is boiled under a reflux for ten to twelve minutes. The contents of the flask are now poured into a large porcelain dish and are allowed to cool, preferably overnight. The potassium salt of benzilic acid soon begins to crystallize and is almost completely precipitated at the end of this time. This salt is filtered off and is washed with a little alcohol. The alcoholic mother liquors, if concentrated, will yield upon standing a small additional amount of potassium salt. The salt is now dissolved in about 3 to 4 l. of water and hydrochloric acid is added slowly with stirring. The portion of the precipitate which is produced by the first 10 cc. of hydrochloric acid (sp. gr. 1.19) is colored reddish brown and is slightly sticky. This should be filtered off; if the procedure has been carried out correctly, the filtrate is nearly colorless. Hydrochloric acid is now added until the precipitation is complete and the benzilic acid is filtered off with suction, washed with cold water until free from chlorides, and dried. The yield is 290 to 300 g. (77–79 per cent theory). The acid is generally a light pinkish yellow and is best purified by recrystallization from benzene. The purification may also be

accomplished by crystallizing from hot water with the use of bone-black or by dissolving in alkali and reprecipitating by means of hydrochloric acid as described above. The product forms needles, m. p. 150°. By boiling the red sticky material which is precipitated by the first portion of hydrochloric acid, with water and 7 g. of bone-black, an additional yield of 10 to 20 g. of pure benzilic acid is obtained.

## 2. Notes

The benzil used must be pure, such as is obtained by recrystallization from alcohol. A number of experiments which were carried out with crude benzil which had merely been washed with water did not give nearly such good yields.

If the potassium salt s not isolated but the reaction mixture is immediately acidified, there is mixed with the benzilic acid a certain amount of benzoic acid which is difficult to remove. This may be done either by fractional solution in sodium carbonate [1] (benzilic acid is a stronger acid than benzoic), by shaking with ligroin,[2] which extracts the benzoic acid from the benzilic, or by boiling with water [3] for some time until the odor of benzoic acid has disappeared. It is better to isolate the potassium salt, since upon acidification very pure benzilic acid is obtained in spite of the fact that it is slightly colored.

In the preparation of certain benzilic acid derivatives from substituted benzils, it has been found that simply dissolving the substituted benzil in alcoholic alkali is sufficient to complete the conversion and no heating is required. With unsubstituted benzil, however, a much poorer yield of benzilic acid is obtained if the reaction mixture is not heated. Longer heating than that given in the directions is likely to decompose some of the product to benzoic acid.

The amount of alcohol and the concentration is such that the maximum amount of potassium benzilate will crystallize out.

[1] Ann. **155**, 79 (1870).

[2] Ann. **356**, 71 (1907).

[3] E. Fischer's "Anleitung zur Darstellung Organischer Präparate" 8th edition, p. 36.

If more alcohol is used in proportion to the water, a large amount of potassium salt crystallizes during the heating and this is objectionable, while less alcohol holds in solution a considerable amount of potassium benzilate and thus decreases the yield.

Benzilic acid is soluble to the extent of 2 per cent in hot water and 0.1 per cent in cold water. By using 20 per cent alcohol, the solubility is increased so that from 100 cc. of solvent 5 g. of pure product may be obtained. Stronger alcohol is not a suitable solvent as the benzilic acid separates from it as an oil. Benzene is the most satisfactory solvent, since 100 cc. dissolve 15 g. at the boiling temperature and yield 13 g. of pure product on cooling.

Sodium hydroxide is not suitable since the sodium salt of the benzilic acid does not crystallize from the reaction mixture.

The 10 cc. of hydrochloric acid specified in the above directions as the amount necessary to precipitate the reddish impure material is an average quantity. In some experiments a little more hydrochloric acid, in some a little less is needed; a pale straw colored liquid should result after the first oil has been precipitated.

### 3. Other Methods of Preparation

Benzilic acid has been made by the action of potassium hydroxide on benzil, either in concentrated aqueous solution [1] (described first in a paper by M. Bösler and later in papers by H. Klinger and by H. Staudinger) or in alcoholic solution [2] (described by J. Liebig, N. Zinin, A. Jena and H. v. Liebig) and either one of these processes furnishes a method for producing benzilic acid cheaply and in large amounts. The other methods by which it may be made are the action of alcoholic potash upon isobenzil; [3] the hydrolysis of diphenyl-bromoacetic acid; [4] the action of alkalies upon benzoin; [5] the action of sodium on benzophenone. [6]

[1] Ber. **14**, 326 footnote (1881); **22**, 1212 (1889); Ann. **356**, 71 (1907).

[2] Ann. **25**, 27 (1838); **31**, 329 (1839); **155**, 79 (1870); especially Ber. **41**, 1644 (1908).

[3] Ber. **19**, 1863 (1886). [4] Ann. **171**, 131 (1873). [5] Ber. **19**, 1868 (1886).

[6] Am. Chem. J. **29**, 607 (1903).

The action of alcoholic potash on benzil has been chosen for special study since less impurity is formed than when aqueous potash is used. The benzilic acid made by the aqueous alkali method is generally deeply colored and the color is rather difficult to remove.

Although the yields with this aqueous alkali method are high with small runs, they decrease when 300 to 500 g. of benzil are used; moreover, the danger of contamination with benzoic acid is always greater. It was found that with runs of 350 to 500 g. of benzil, the yields of benzilic acid, using the alcoholic alkali method of H. v. Liebig given above, were never as good as those described in the literature; with small amounts of material (up to 100 g.) however, yields often over 90 per cent were obtained. It has been stated in the literature [1] in one of the more recent articles (using aqueous potassium hydroxide) that occasionally poor runs resulted, and it has been found in this investigation that every now and then a low yield will result.

[1] Ann. 356, 71 (1907).

# VI

## BENZOIN

$$2C_6H_5CHO + (NaCN) \rightarrow C_6H_5CHOHCOC_6H_5$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by J. B. CONANT and C. E. BILLS.

### 1. Procedure*

IN a 3-l. round-bottom flask fitted with a reflux condenser, 625 cc. of alcohol (95 per cent), 500 cc. of water, 500 g. of pure benzaldehyde and 50 g. of sodium cyanide (96–98 per cent) are placed. This mixture is then heated and kept boiling for 0.5 hour. In the course of about twenty minutes, crystals begin to separate from the hot solution. At the end of the thirty minutes, the solution is cooled, filtered with suction, and washed with a little water. The yield of dry crude benzoin, which is white or light yellow, amounts to 450 to 460 g. (90–92 per cent theory). In order to obtain it completely pure, the crude substance is recrystallized from alcohol, 90 g. of crude material being dissolved in about 700 cc. of boiling alcohol; upon cooling, a yield of 83 g. of white, pure benzoin is obtained, m. p. 129°.

### 2. Notes

It is absolutely necessary that pure benzaldehyde be used for this reaction. The crude benzaldehyde which is obtained on the market should be washed with sodium carbonate solution, dried, distilled, and a fraction collected at 178–180°. Crude material will never give much more than a 50 per cent yield of benzoin.

The above directions require 50 per cent of the amount of dilute alcohol which is ordinarily recommended in the literature.

* See Org. Syn. 6, 103, for a slight change in procedure.

This allows one to prepare just double the amount of material in the same sized flask. The product obtained in this way, however, is slightly yellower than that obtained when more alcohol is used, but upon recrystallization it gives just as pure a product as that obtained by recrystallization of crude material made in the presence of more solvent. The results of many experiments lead to the conclusion that if large amounts of benzoin are to be prepared, the method described above is the better one. If, however, only a small amount is needed and a good grade of crude material is satisfactory, the larger amount of solvent is perhaps more desirable.

Several times when benzoin was being prepared, the condensation took place and was complete after boiling five to ten minutes or even less, the product separating out in the hot solution with evolution of heat. The yield under these conditions was always good and the color better than when the reaction took a longer time. The cause of this occasional rapid reaction was not discovered, but it was probably due to inoculation with a little benzoin in certain of the experiments. When it takes place as just described, the flask and efficient condenser used will be sufficient to condense the sudden, rapid evolution of alcohol vapors caused by the heat of crystallization of the benzoin.

### 3. Other Methods of Preparation

The only good method for the preparation of benzoin[1] appearing in the literature is by the action of potassium cyanide upon an alcoholic solution of benzaldehyde, a method described first by Wöhler and later modified slightly by Zinin and Zincke. The other methods are of theoretical importance only and have, therefore, not been studied. Thus, by the reduction of benzil,[2] and by the oxidation of hydrobenzoin,[3] benzoin can be formed; it happens, however, that both benzil and hydrobenzoin are commonly made from benzoin.

[1] Ann. **3**, 276 (1832); **34**, 186 (1840); **198**, 151 footnote (1879); discussion of mechanism of reaction, Ber. **21**, 1346 (1888); Ann. **298**, 312 (1897); J. Chem. Soc. **83**, 1004 (1903).

[2] Ann. **119**, 177 (1861).

[3] Ann. **198**, 123 (1879).

## α-BROMONAPHTHALENE

$$C_{10}H_8 + Br_2 \rightarrow C_{10}H_7Br + HBr$$

Prepared by H. T. CLARKE and ETHEL SCHRAM.
Checked by ROGER ADAMS and M. E. MORALES.

### 1. Procedure

IN an 8-l. crock are placed 2320 g. of naphthalene (flakes) and 2.5 l. of hot water. The temperature is brought to 40–50° and the mixture is vigorously stirred mechanically, while to it are added slowly 2900 g. (900 cc.) of bromine from a dropping funnel, the stem of which reaches to the bottom of the crock. No water jacket is necessary, the temperature of the mixture being kept at 40–50° by regulating the rate of addition of the bromine. The addition takes eight to nine hours but requires practically no attention. When all the bromine has been added, stirring is continued until the color has practically disappeared, at which time the mixture is allowed to cool and the heavy oil is separated. It is then heated in a 5-l. flask to 145–150° (oil bath) and a current of dry steam is passed in until 3 l. of distillate have been collected. This treatment eliminates hydrobromic acid from the bromine addition products and also removes some of the unchanged naphthalene.

The oil is then fractionally distilled under reduced pressure, and the main fraction which passes over at 132–135° at 12 mm. (145–148° at 20 mm.) is collected separately. The fore-runs on chilling yield naphthalene, which is filtered off and the filtrate is again distilled. The higher boiling portions on chilling yield dibromonaphthalene and the filtrate is again fractionated.

The united water solutions are distilled and 48 per cent hydrobromic acid boiling at 125–126° is collected. The yield of pure α-bromonaphthalene varies from 2000 to 2200 g. and in certain cases reaches 2450 g., the yield of hydrobromic acid amounting to about 2650 g.

## 2. Notes

It is essential that the stirring should be efficient. A glass stirrer of the tube or propeller type answers satisfactorily, provided that the naphthalene flakes are not too coarse. As the reaction proceeds the product becomes oily, rendering the stirring more efficient.

The necessity of introducing the bromine at the bottom of the mixture should be emphasized. If this is not done, local overheating is almost certain to occur, with consequent loss of both bromine and hydrobromic acid.

If the distillation of α-bromonaphthalene is carried on at atmospheric pressure, the product darkens on standing, but it does not do so if distilled under reduced pressure.

The higher boiling solid by-product contains, among other substances, 1, 4-dibromonaphthalene melting at 79–80°. This can be isolated by repeated recrystallization from carbon tetrachloride, but so many crystallizations are necessary that the final yield is low.

## 3. Other Methods of Preparation

α-Bromonaphthalene has been prepared by the action of bromine upon naphthalene without a solvent;[1] by the action of bromine upon naphthalene in carbon disulfide;[2] by treating a suspension of naphthalene in a solution of bromine in alkali with hydrochloric acid;[3] by the action of cyanogen bromide upon naphthalene at 250°;[4] by the action of bromine upon mer-

[1] Z. Chem. **1865**, 3.
[2] Ann. **135**, 40 (1865); **147**, 166 (1868).
[3] Ber. **15**, 2721 (1882).
[4] Ber. **10**, 756 (1877).

cury dinaphthyl;[1] by the removal of the amino group from $\alpha$-bromo-$\beta$-naphthylamine by diazotization.[2]

As methods of preparation, only the first three need be considered. It was decided not to try the direct action of bromine upon naphthalene, owing to the necessity of stirring the solid naphthalene and of collecting the hydrogen bromide gas; the latter difficulty is also presented when carbon disulfide is used, and the objectionable properties of this solvent make its use further unfavorable. The third method, in which a suspension of naphthalene in alkaline hypobromite solution is treated with hydrochloric acid in aqueous solution, was found to give satisfactory results in so far as the yield of $\alpha$-bromonaphthalene is concerned (though it was no better than with the method above described), but it presented considerable difficulties in the recovery of the hydrobromic acid.

[1] Ann. **147**, 175 (1868).

[2] Ber. **4**, 851 (1871).

## VIII

# *p*-BROMOPHENOL

$$C_6H_5OH + Br_2 \rightarrow (p)BrC_6H_4OH + HBr$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by OLIVER KAMM and R. W. HUFFERD.

## 1. Procedure

IN a 5-l. round-bottom flask fitted with a rubber stopper, holding a mechanical stirrer (Fig. 1, p. 4), reflux condenser and separatory funnel, are placed 1 kg. of phenol dissolved in 1 l. of carbon disulfide. To the top of the condenser is attached a calcium chloride tube and from this a glass tube leads into a beaker holding about 1200 cc. of cracked ice and water for the absorption of the hydrobromic acid evolved. In the separatory funnel are placed 1702 g. (546 cc. at 20°) of bromine dissolved in 500 cc. of carbon disulfide. The flask is well cooled (below +5°) in a salt and ice mixture, stirring is started, and the bromine solution is allowed to run in. The addition requires about two hours. When this is completed, the flask is disconnected and a condenser set for downward distillation is attached to it. By having a boiling flask as a receiver attached tightly to the lower end of the condenser, the dissolved hydrobromic acid which is evolved at the beginning of the heating may be led into the water used for collecting the first hydrobromic acid. The carbon disulfide is distilled off, and amounts to about 1200 cc. The residual liquid is then slowly distilled *in vacuo* with a good fractionating column in a 1.5- or 2-l. Claisen flask which must be slightly modified (Fig. 3, p. 40, see also Notes) so that the *p*-bromophenol after coming in contact with cork or rubber will not be carried into the condenser; if it does, it becomes pink-

ish. There are obtained from various runs 1475 to 1550 g. (80–84 per cent theory) of *p*-bromophenol boiling 145–150° at 25–30 mm., 250 to 350 g. of lower boiling material consisting of a mixture of *o*-bromophenol and *p*-bromophenol from which it is very difficult to extract either constituent in pure form, and finally a small quantity of high-boiling material consisting chiefly of 2, 4-dibromophenol. The *p*-bromophenol on cooling solidifies to a

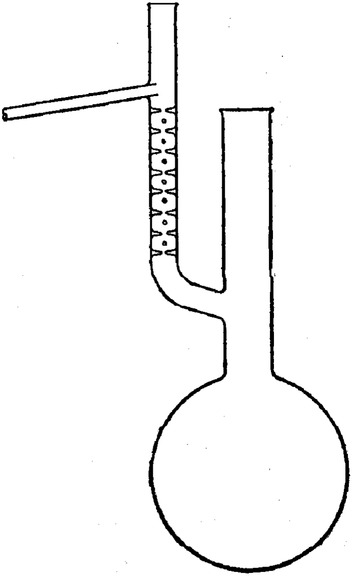


FIG. 3.

solid white mass containing practically no oil. By centrifuging the product, perfectly dry white crystals are obtained, m. p. 63°. There is also produced in this preparation about 1.5 to 1.6 l. of hydrobromic acid with a sp. gr. of about 1.3.

## 2. Notes

Although it is not absolutely necessary that the reaction mixture be cooled with salt and ice, it is highly desirable, since

this reduces the amount of *o*-bromophenol and hence the amount of low-boiling fraction; the recovery of carbon disulfide is also more satisfactory. A run of the same size as is described above was made, keeping the solution at room temperature, and under these conditions the yield of pure *p*-bromophenol was diminished.

The loss of carbon disulfide is due to its great volatility, the consequent passing off with the hydrobromic acid and the general loss during experimental manipulations.

The experiments may be run with a larger amount of carbon disulfide with satisfactory results. This, however, involves a longer time for distillation and is therefore undesirable. More concentrated solutions were not tried.

Moisture prevents the *p*-bromophenol from crystallizing, so that particular care should be taken to keep it out of the reaction mixture.

A complete run may be made in less than five hours.

The *p*-bromophenol if distilled without using a fractionating column and collected over a 5° range as already described will generally amount to 1600 to 1660 g. (87–90 per cent theory). This material on cooling, however, never solidifies completely but always contains a certain amount of oil; it is satisfactory for most purposes, just as it is. Even though the once-distilled material may be freed from oil and then redistilled without special fractionation, some oil remains. To obtain a very pure product this material must be cooled to 10° and then centrifuged. In this way, hard white crystals which melt sharply at 63° result. During this process about 15–20 per cent of the product goes to the filtrate which, however, can be chilled again so that a certain amount of pure *p*-bromophenol may be obtained from it. Although a number of solvents were used in an attempt to crystallize *p*-bromophenol, none was found which was entirely satisfactory.

The flask shown in Fig. 3 (p. 40) is particularly suited for distilling any liquids which have a great tendency to attack rubber or cork. It is a modification of one already described in the literature;[1] the side-arm outlet tube extends a short distance

[1] J. Am. Chem. Soc. **39**, 2718 (1917).

into the neck of the flask, thus preventing any vapor which has touched the cork or rubber from condensing and flowing down the side-arm into the receiver. This same device may, of course, be applied to any type of distilling flask.

### 3. Other Methods of Preparation

The methods for producing *p*-bromophenol are: the action of bromine on phenol in carbon disulfide;[1] the action of bromine on phenol in glacial acetic acid;[2] the action of bromine on phenol in a mixture of sulfuric acid and acetic acid;[3] the distillation of bromosalicylic acid with barium oxide and sand;[4] the action of bromocyanogen on phenol;[5] the diazotization of *p*-bromoaniline and subsequent heating with water.[6] Holleman[7] and Rinkes have recently studied the bromination of phenol in water, carbon tetrachloride, carbon disulfide and glacial acetic acid in order to determine the proportion of *o*- and *p*-bromophenols which are produced. Of the organic solvents there is little preference, as the maximum yield of para derivative in any of the solvents under ordinary conditions varies between 85 and 92 per cent. The temperature, however, has a marked effect. In carbon disulfide which seems to be slightly better than the other solvents, the yield of the para derivative varies from 97.3 per cent at $-30°$ to 86.2 per cent at $+30°$.

In this investigation, the methods using bromocyanogen or bromosalicylic acid were not considered on account of the expense of raw materials. The diazotization of *p*-bromoaniline was studied, chiefly because it was anticipated that a very pure *p*-bromophenol might be obtained. This, however, was not the case, and, moreover, the yields were poor. The bromination of phenol in glacial acetic acid is satisfactory except that the acetic acid cannot be recovered conveniently. The bromination

[1] Ann. **137**, 200 (1866); Ber. **28**, 978 (1895).
[2] Ber. **6**, 171 (1873); Ann. **234**, 138 (1886).
[3] J. Chem. Soc. **85**, 1227 (1904).
[4] Ann. **52**, 338 (1844).
[5] Ber. **33**, 1555 (1900).
[6] Ber. **7**, 1176 (1874).
[7] Rec. trav. chim. **30**, 49 (1911).

in sulfuric acid (75 per cent) is unsatisfactory since the phenol does not dissolve readily at 0° and if a temperature high enough to dissolve it is used, a considerable amount of *o*-bromophenol is produced. As for the other solvents, carbon tetrachloride might seem preferable to carbon disulfide on account of its non-inflammability. It is not as good, however, as carbon disulfide, since it must be used in much larger amounts to dissolve the phenol at 0°, and since it is much less easily removed and the proportion of *o*-bromophenol is slightly greater.

# IX

## DIACETONE ALCOHOL

$$2CH_3COCH_3 + [Ba(OH)_2] \rightarrow (CH_3)_2COHCH_2COCH_3$$

*Prepared by* J. B. CONANT *and* NEAL TUTTLE.
Checked by ROGER ADAMS and H. C. N. HECKEL.

### 1. Procedure

A 2-l. round-bottom flask is fitted with a rubber stopper carrying a Soxhlet extractor which in turn is fitted with an efficient reflux condenser. 1500 cc. (1190 g.) of acetone (commercial grade) is placed in the flask and a few pieces of broken tile are introduced to produce even boiling. Two of the usual paper thimbles are placed in the extractor, one above the other. The lower one is filled nearly full of barium hydroxide; the top one is filled about three-quarters full of the same substance, and the remainder of the space is filled with glass wool. The flask is heated on a steam bath or in an oil bath. The heat is so regulated that the acetone refluxes back into the extractor rather rapidly. As the reaction proceeds the boiling-point of the mixture rises and more steam has to be turned on or the temperature of the oil bath has to be raised. The flask should finally be lowered as far as possible into the cone of the steam bath. The reaction is complete when the liquid no longer boils when heated as hot as possible on the steam bath. This usually requires ninety-five to one hundred and twenty hours. The refluxing may be interrupted at any time for as long as desired. The liquid in the flask has now a sp. gr. of about 0.91 (20°) which corresponds to about 80 per cent of diacetone alcohol. The only loss of material is by volatilization of the acetone through the top of the condenser; this generally amounts to several per cent.

The crude diacetone alcohol is purified by distillation. The 2-l. round-bottom flask is fitted with a three-bulb Glinsky fractionating column and a well-cooled condenser. The flask is heated in an oil bath, the temperature of which is gradually raised to 125°. The temperature of the bath is held at this point until no more acetone distils over, the temperature at the top of the column registering about 70° when the process is complete. The recovered acetone, containing a few per cent of diacetone alcohol, amounts to about 200 g. and can be used to prepare more material. The residual liquid has a sp. gr. of 0.928 (20°) and contains about 95 per cent of diacetone alcohol. It is transferred to a 2-l. Claisen flask and distilled under diminished pressure. A little acetone first comes over and then the diacetone alcohol distils smoothly at 71–74° at 23 mm. The yield is 850 g. (71 per cent of the theory based on the total acetone employed). The entire distillation requires about four hours.

## 2. Notes

Almost any form of a Soxhlet extractor and condenser will serve. It is advisable to use as much barium hydroxide as possible and to have the extractor empty as often and as completely as possible. The use of glass wool and care in filling the cups prevents any solid hydroxide from being carried down into the lower flask.

The use of tartaric acid in the flask has been recommended to neutralize any barium hydroxide that is carried down. This has been found unnecessary.

If hydrated barium hydroxide [$Ba(OH)_2 \cdot 8H_2O$] is used in the thimbles this becomes dehydrated after one run; the anhydrous form is just as satisfactory and may be used over and over again.

The time of refluxing depends on the rapidity with which the liquid boils and on the way in which the Soxhlet extractor empties. Similarly, the point at which the liquid ceases to boil will vary somewhat with the way in which it is heated. The

amount of diacetone alcohol produced will, thus, vary somewhat in similar experiments. Refluxing for forty to fifty hours produces about a 70 per cent mixture which is perfectly suitable for preparing the pure product, except that more acetone is recovered unchanged.

Acetone and diacetone alcohol are in equilibrium with each other. The speed of both reactions is greatly accelerated by the presence of a base. The equilibrium mixture contains only a few per cent of diacetone alcohol but the dissociation of diacetone alcohol to acetone proceeds so slowly in the absence of barium hydroxide that it is possible to increase the concentration to 80 per cent by this procedure.

With some samples of commercial acetone containing considerable water, it has been found advisable to dry the acetone first with calcium chloride. This is usually not necessary.

The final distillation of diacetone alcohol must be carried out under diminished pressure as otherwise some of the material decomposes into acetone.

### 3. Other Methods of Preparation

The methods for producing diacetone alcohol are: the action of barium hydroxide on acetone; [1] the action of calcium hydroxide on acetone; [2] the action of concentrated sodium hydroxide or potassium hydroxide on acetone; [3] the action of magnesium amalgam on acetone; [4] and the action of nitrous acid on diacetonamine.[5] The last method was not considered because of the difficulty of preparing diacetonamine. Of the methods employing acetone only, the first two seemed more promising, since the others are reported as giving low yields of impure product. It was soon found that barium hydroxide acted more rapidly than calcium hydroxide (as reported by L. P. Kyriakides) and this method was therefore employed.

[1] J. Am. Chem. Soc. **36**, 534 (1914).

[2] D. R. P. 229,678; Frdl. **10**, 998 (1910–12); C. A. **8**, 788 (1914); U. S. pat. 1,550,702 (1925); C. A. **20**, 51 (1926).

[3] Ann. **169**, 114 (1873); Z. physik. Chem. **33**, 130 (1900); Ann. chim. phys. (9), **19**, 32 (1923).

[4] Ann. chim. phys. (8), **21**, 411 (1910).

[5] Ann. **178**, 342 (1875); Ber. **34**, 2856 (1901).

# X

## FURFURAL

$$C_5H_{10}O_5 \rightarrow C_4H_3OCHO + 3H_2O$$

Prepared by ROGER ADAMS and V. VOORHEES.
Checked by H. T. CLARKE and E. R. TAYLOR.

### 1. Procedure*

IN a 12-l. round-bottom flask are placed 1500 g. of corn cobs (ground to about the size of corn kernels), 5 l. of 10 per cent sulfuric acid and 2 kg. of salt. The flask is shaken in order to secure a homogeneous mixture and is then connected with an upright tube water condenser and return tube as shown in Fig. 4 (p. 50). Heat is applied from a ring burner, the flame being adjusted so that the liquid distils at a rapid rate.

The distillation process is continued until practically no more furfural can be seen collecting in the distilling flask used as a receiver. The above operation requires from five to ten hours.

This distillate is now treated with enough sodium hydroxide so that the mixture is left just faintly acid and the furfural separated. It amounts to 180 to 220 g. The wet furfural is distilled under diminished pressure from a Claisen flask which is heated in an oil-bath. The temperature of the bath is never permitted to rise above 130°. At first, water together with some furfural distils, and this fraction is separated to be worked up with a later portion. Finally, pure furfural (b. p. 90° at 65 mm.) distils and this fraction, collected separately, is found to be practically colorless. Its boiling point at 745 mm. is 159°. The distillation of the crude material must not be carried out under ordinary pressure, or else the product turns dark rapidly

* A slight change in the method of collecting the furfural is described in Org. Syn. 6, 103.

on standing. After one vacuum distillation as described, however, a distillation under atmospheric pressure may be carried out without the objectionable results just mentioned.

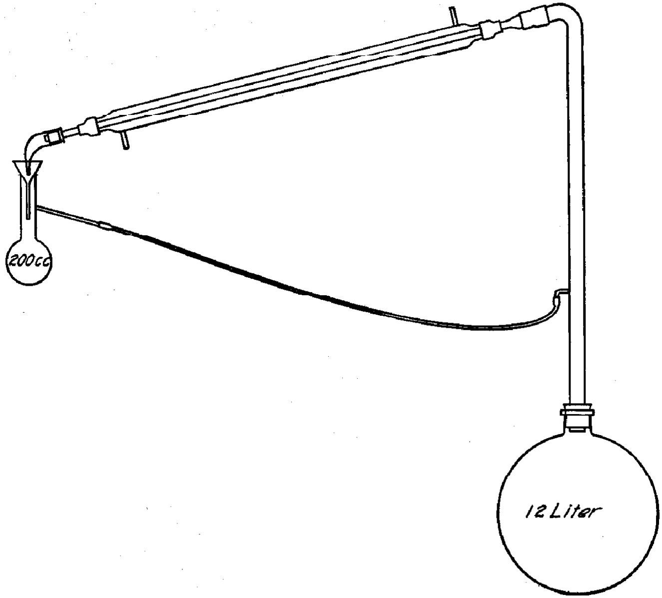



FIG. 4.

## 2. Notes

Vacuum distillation of the product is essential. Moreover in this final distillation the precautions mentioned (the use of an oil-bath and an outside temperature of less than 130°) must be carefully observed. When the furfural is distilled under ordinary pressure or when it is distilled under diminished pressure with a free flame, a practically colorless product is at first obtained. After a few days and sometimes after a few hours this product will gradually darken until finally a black liquid results. This change, although most marked in the presence of light, takes

place readily even when the aldehyde is stored in brown-glass bottles. On the other hand, when the crude furfural is distilled under diminished pressure and is never heated above 130° during the process of distillation, a product is obtained that develops only a slight color when exposed to direct sunlight during several days. Further purification according to methods described in the literature does not give a product which will remain colorless on standing.

Certain samples of ground cobs which had remained in the laboratory for a year did not give nearly such good yields of furfural as those which were fresher.

The apparatus described (Fig. 4, p. 50) is a very convenient one for laboratory use but may be modified in many ways as long as a few essential points are kept in mind. A modification worth mentioning is the use as a receiver of a vessel the bottom of which has a stop-cock attached, thus allowing the furfural to be drawn off at any time. It is necessary to have the receiver several inches higher than the opening in the upright tube so that the aqueous liquors will flow back to the reaction flask; the lower end of the funnel in the receiver must be below the side arm of the receiver in order to prevent bubbles of furfural from collecting on the surface of the liquid and being carried back to the reaction flask; the entrance of the returning liquid into the upright tube must be at such a point that a vigorous stream of vapor passes through the returning liquid, thus extracting much of the furfural carried back in the water; the tube for returning the aqueous liquors must at some point be lower than the entrance to the upright tube so that a trap of liquid will be formed and prevent the vapors from the reaction flask entering the side tube. If the return tube is small and swings too low, it happens occasionally that a bubble of air gets into the tube and prevents the regular flow of liquid; this can be remedied by shaking the tube till the difficulty is overcome. It was found that the more efficient the upright tube was as a fractionating column, the more complete was the separation of furfural.

### 3. Other Methods of Preparation*

Furfural occurs in many essential oils and is produced in small quantities in many organic reactions,[1] particularly those involving the decomposition of various carbohydrate materials. Pentoses when subjected to the action of hydrochloric acid are decomposed to give practically quantitative yields of this aldehyde.[2] It is well known that carbohydrate materials such as corn cobs, wood, bran, etc., when heated with steam under pressure or distilled with dilute hydrochloric or sulfuric acids, yield appreciable quantities of furfural.[3] Particularly good yields, however, are obtained from ordinary corn cobs, and this material therefore appears best for the production of large amounts of furfural in the laboratory. Improvements in the production of furfural from carbohydrate material have appeared recently in the patent literature[4] but those do not appear as satisfactory as the ones described.[5]

* Recent methods of preparation through 1925 are described in Org. Syn. **6**, 106.

[1] E. Abderhalden's Biochemisches Handlexicon Vol. I (2), 853, gives an extensive review of the literature of furfural together with numerous references.

[2] Am. Chem. J. **13**, 73 (1891); J. Anal. Appl. Chem. **5**, 421 (1891); Ber. **24**, 3019 (1891).

[3] Am. Chem. J. **13**, 348 (1891); Ann. **74**, 280 (1850); **116**, 258 (1860); **150**, 197 (1870); **249**, 237 (1888); **260**, 291 (1890); Ber. **28**, 1940 (1888); Am. Chem. J. **3**, 33 (1881); "Organic Chemistry for the Laboratory" by W. A. Noyes (1920) p. 191; J. Ind. Eng. Chem. **13**, 133 (1921); Z. angew. Chem. **27**, 654 (1914).

[4] C. A. **13**, 1863 (1919).

[5] U. S. Patent Pending.

# XI

## MESITYL OXIDE

$$(CH_3)_2COHCH_2COCH_3 + (I_2) \rightarrow (CH_3)_2C=CHCOCH_3 + H_2O$$

Prepared by J. B. CONANT and NEAL TUTTLE.
Checked by ROGER ADAMS and H. C. N. HECKEL.

### 1. Procedure

A 1-l. round-bottom flask is fitted with a three-bulb Glinsky fractionating column connected to a water-cooled condenser set for distillation. The crude diacetone alcohol prepared as previously directed (Exp. IX, p. 45) and 0.1 g. of iodine are placed in the flask. The crude alcohol will usually weigh about 1100 g. and will have a sp. gr. of about 0.91. The mixture is now distilled steadily but not too rapidly with a small free flame and three portions are collected as follows: I. 56–80°; II. 80–126°; III. 126–131°. The first portion is acetone containing a small amount of mesityl oxide and water; it can be used again for preparing more crude diacetone alcohol. The second portion separates into two layers,—water and crude mesityl oxide. The third portion is pure mesityl oxide. While the third fraction is distilling, the aqueous layer in fraction II is separated in a separatory funnel and the crude mesityl oxide is dried with anhydrous calcium chloride. This crude mesityl oxide is then distilled through a Glinsky column, and by this means a further amount of acetone and a small intermediate fraction (85–126°), which is best discarded, are separated. The pure mesityl oxide itself then distils between 126–130° and is added to the pure product already obtained as the third portion of the first distillation. The first complete distillation will require about five hours; the redistillation of portion III will

take about one hour. The yield is 650 g. (65 per cent of the theory based on the total acetone employed). About 300 g. of acetone are recovered.

## 2. Notes

The crude diacetone alcohol is prepared according to the directions in Exp. IX (p. 45). The acetone recovered from the preparation of mesityl oxide can be mixed with fresh acetone and successfully used in preparing more crude diacetone alcohol.

If the crude diacetone alcohol does not contain as much as 80 per cent of diacetone alcohol (if the refluxing is not carried out long enough, for example) the yield of mesityl oxide will be, of course, correspondingly low.

The first distillation should not be interrupted but should be carried out at a slow uniform rate until the distillation is complete.

The very last portion of fraction III is sometimes slightly colored, apparently by some iodine, which comes over at the end of the distillation. A small amount of high-boiling residue is always left.

## 3. Other Methods of Preparation

The methods of making mesityl oxide fall into three classes: (1) the action of condensing agents (hydrochloric acid, etc.) on acetone;[1] (2) the dehydration of diacetone alcohol;[2] (3) and from diacetonamine.[3] The latter method was not considered since the amine is relatively difficult to prepare. The action of acid condensing agents on acetone is very unsatisfactory; the yields are poor and considerable quantities of phorone and similar substances are invariably produced. The direct production

[1] Am. Chem. J. **19**, 887 footnote (1897); Ann. **110**, 32 (1859); **178**, 343 (1875); **180**, 4 (1875); **188**, 131 (1877) J. Am. Chem. Soc. **35**, 1061 (1913); Compt. rend. **140**, 721 (1905); Ber. **41**, 574 (1908); Bull. soc. chim. (4) **3**, 829 (1908); for further references see Org. Syn. **6**, 107.

[2] Ann. **178**, 351 (1875); J. Am. Chem. Soc. **36**, 534 (1914); **37**, 1748 (1915); Monatsh. **34**, 779 (1913); Chem. Zentr. 80 (I), 1282 (1909); Frdl. **9**, 62 (1907–10); D. R. P. 208,635.

[3] Ber. **7**, 1387, 1777 (1874); Ann. **174**, 156 (1874).

of mesityl oxide from acetone and calcium oxide[1] was tried, but without success; diacetone alcohol was the principal product.

Several methods which have been proposed for the dehydration of diacetone alcohol were investigated. H. Hibbert's method[2] (using a very small quantity of iodine) is superior to either the action of concentrated sulfuric acid or aluminum phosphate. The reaction proceeds more easily and the product is purer; this method has therefore been adopted.

[1] J. Am. Chem. Soc. **31**, 722 (1909); **Frdl. 11**, 46 (1912–14); **D. R. P.** 258,057.
[2] J. Am. Chem. Soc. **37**, 1748 (1915).

XII

# METHYLENE IODIDE

$$CHI_3 + Na_3AsO_3 + NaOH \rightarrow CH_2I_2 + NaI + Na_3AsO_4$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by H. T. CLARKE and KATHARINE OGDEN.

## 1. Procedure

IN a 5-l. round-bottom flask fitted with a rubber stopper holding a mechanical stirrer (Fig. 1, p. 4), a reflux condenser, a separatory funnel and a thermometer with bulb under the liquid, 1 kg. of iodoform is placed. To this are added 500 cc. of the sodium arsenite solution (prepared from 274 g. (1.5 mole) of arsenious oxide, 532 g. (7 moles) of sodium hydroxide and 2600 cc. of water). Stirring is started and heat is applied until the temperature of the thermometer reaches 60–65°, where it is held constant during the whole reaction. If the temperature is allowed to go much higher, especially at the beginning of the experiment, the reaction becomes too vigorous, and at the same time a little methyl iodide is formed. The remainder of the sodium arsenite solution is added gradually during the course of one-half an hour. The whole mixture is then kept one hour at 60–65° to be sure that the reaction is completed. The reaction mixture is allowed to cool somewhat (to about 40°) and is filtered with suction in order to remove the mechanical impurities which have come from the technical arsenious oxide and sodium hydroxide. The filtrate consists of a clear water solution with a pale yellow oil underneath. It is better not to allow the reaction mixture to cool completely before filtering or else a precipitate of sodium arsenate will gradually separate and this will tend to make an emulsion of the methylene iodide and hinder filtration and sep-

aration. The methylene iodide is now separated from the filtrate, is dried with a little calcium chloride and is distilled *in vacuo*. Practically all of it comes over as a light straw-colored oil between 106–107° at 70 mm., the bath being kept at 130–135°. The yield of crude product is 610 to 660 g. (90–97 per cent theory). By distillation, not more than 10 to 20 g. are lost. The crude product is quite satisfactory for most purposes. The methylene iodide obtained after distillation in vacuo melts at 6°.

## 2. Notes

Experiments were made on 100 g. lots of iodoform, using varying amounts (between 1 mole and 2 moles) of sodium arsenite. The yield is, in general, best when only a very slight excess over 1 mole of arsenious oxide is used. In every case the amount of sodium hydroxide employed was that called for by the theory.

The dilution of the solution makes very little difference, the yields remaining about the same. It is, therefore, better to use as concentrated a solution as possible so that large runs may be made in a comparatively small apparatus. A more concentrated solution, however, than the one advised above is not satisfactory, since too much sodium arsenate tends to separate out during the cooling after the methylene iodide has formed and causes some trouble in the purification. If sodium arsenate does separate, the methylene iodide is obtained either by distilling with steam, or by diluting and boiling to dissolve the crystals, this last to be followed by filtering and separating.

Mechanical stirring is quite necessary in order to get the best yields in the shortest time.

In making methylene iodide from 100 g. lots of iodoform or even 200 g. lots, the sodium arsenite solution may be added all at once. When the runs become larger, however, it is inadvisable to do this and directions similar to those described above in running a kg. of iodoform must be used.

After vacuum distillation, a residue of 1 to 2 g. is left in the flask. When air is admitted to the flask, a single flash of light sometimes occurs. In one case, the thermometer and stopper were even blown off the flask. The cause was not determined.

If the reaction is carried out at refluxing temperature instead of at 60–65°, the yield of product is diminished by 5–10 per cent, the formation of a little methyl iodide accounting for the loss.

### 3. Other Methods of Preparation

Three common methods of production are described in the literature; the action of iodine,[1] sodium ethylate,[2] or hydriodic acid[3] on iodoform. The last of these three methods has been worked out in more detail and is the one generally recommended for the preparation of methylene iodide in the laboratory. In addition, methylene iodide has been produced by the action of iodine on diazomethane[4] and by electrolysis of iodoacetic acid.[5] It may also be made by the action of potassium iodide upon methylene chloride.[5a]

The reduction of iodoform by means of sodium arsenite,[6] described both by V. Auger and A. Gutmann, gave such successful results that the other methods were disregarded. The reaction is extremely simple and in the course of a few hours several pounds of pure methylene iodide may be prepared.

[1] Ann. **115**, 267 (1860).
[2] Ann. chim. phys. (3) **53**, 313 (1858).
[3] Z. Chem. **1868**, 712; Ber. **5**, 1095 (1872).
[4] Ber. **27**, 1889 (1894).
[5] Ber. **42**, 3869 (1909).
[5a] J. Chem. Soc. **119**, 1400 (1921).
[6] Compt. rend. **145**, 810 (1907); **146**, 1282 (1908); Ber. **52**, 212 (1919).

XIII

# METHYL HEXYL CARBINOL (CAPRYL ALCOHOL)

$$CH_3(CH_2)_5CHOHCH=CH(CH_2)_8CO_2Na+NaOH+H_2O \rightarrow CH_3(CH_2)_5CHOHCH_3+NaO_2C(CH_2)_8CO_2Na+H_2.$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by OLIVER KAMM and W. S. MARLOTH.

## 1. Procedure

FOR the most satisfactory preparation of methyl hexyl carbinol from castor oil, a copper vessel should be used. Since such a vessel is often not available in the average laboratory, directions are also included using an ordinary can, although in such cases the yields are much lower.

In a large dish pan, 1900 g. of No. AAA castor oil are treated with occasional stirring with a solution of 500 g. of technical (93–95 per cent) sodium hydroxide in 300 cc. of water. A reaction takes place, some heat is developed, and within ten or fifteen minutes a very hard solid soap is produced. This soap is broken up into small pieces and placed in a 3-gallon can. In this preparation, a petroleum ether can was used, but any kind available would be just as satisfactory. The container is now fitted with an efficient reflux condenser and it is then heated over a ring burner as long as hydrogen is given off. The heating is regulated to produce a fairly rapid evolution of gas as shown by leading a tube from the top of the condenser into a small beaker of water. The time required for the complete evolution of the hydrogen is about nine to ten hours.

If the above reaction is not completed at one time and intermediate cooling is allowed, the reaction mixture sets to a solid mass and certain precautions must be taken before proceeding farther. Either before heating is renewed, the mass must be

punched full of holes by means of an iron rod, or when the heating is started care must be taken to heat the upper part of the can first and gradually to approach the bottom. If the under part of the solid soap were heated directly, it would decompose before the upper part, and the hydrogen, being unable to escape, would cause the can to burst.

The condenser is now set downward for distillation and the heating is continued. If intermediate cooling is allowed, one of the precautions mentioned above before starting the distillation, must be observed. The alcohol distils over with the water and is separated from time to time, the water being returned to the distillation can by means of a separatory funnel inserted through a rubber stopper in the top of the can. The addition of this water must be very slow in order to prevent foaming. The heating should be regulated so that the distillate is coming over in rapid drops, not in a stream. If desired, the same sort of gravity separator described below under the large-sized experiment may be used in this small run. About twelve hours are required for this distillation. Toward the end, high-boiling products are obtained and considerable gas is liberated. Dif ficulty is almost always encountered during this part of the preparation since the long heating causes the solder in the bottom edge of the can to melt and leaks thus develop which allow a certain amount of soap to run out. The distillation need not be stopped, because the soap fills the holes, but under these conditions the temperature cannot be maintained at a point high enough for the complete distillation without material loss from increased leakage. The upper layer of crude alcohol is separated from the water and fractionated. The portion boiling from 100–120° is chiefly water with a little alcohol in it. The second fraction between 120–175° contains a considerable quantity of ketones along with the alcohol. The main portion 175–185°, is the methyl hexyl carbinol. Upon refractionation, 190 to 200 g. (23–25 per cent theory) of alcohol boiling at 175–180° are obtained.

This product is satisfactory for most purposes. If, however, a very pure product is desired, this may be made by shaking carefully the alcohol with 15 per cent sodium bisulfite solution.

separating the alcohol and steam distilling it from alkaline solution. The alcohol is finally distilled and the fraction boiling 177–179° is collected. If saturated sodium bisulfite be employed, a crystalline material which contains alcohol is formed and causes difficulty in the separation. Two runs of 6 kg. of castor oil with the same relative proportions of alkali and water were made in 8-gallon cans. The yield in the first case was 650 g. of pure material and in the second case 730 g.

## Preparation in Copper Vessel

To the cover of a 12-gallon copper kettle is fitted an apparatus to which a continuous separator may be attached (Fig. 5, p. 64). This apparatus consists of an upright water condenser through the jacket of which steam is passed; a connecting tube leads from the top of this condenser to a second spiral condenser the bottom of which extends into a gravity separator. This allows the alcohol to run off into a receiver and the heavier aqueous layer to return through a separatory funnel to the copper kettle. A few essential points in the apparatus should be indicated; it is necessary that the return arm of the gravity separator be below the tube through which the alcohol flows into the receiver; the lower end of the funnel must be below the return side-arm in order to prevent water being carried along with the methyl hexyl carbinol; the capillaries A and B are necessary to prevent siphoning in the respective tubes. A soap is made as already described from 11.2 kg. of No. AAA castor oil and 2900 g. of sodium hydroxide in 5800 g. of water. This is broken up, placed in the kettle and gradually heated. Much gas is evolved and care should be taken not to lose alcohol, particularly at the beginning. The separator is not adjusted and the stopcock of the separatory funnel is kept closed until about 3000 cc. of distillate are collected; any small amount of alcohol is separated and the water discarded. The separator is now put in place to return the water to the kettle. The separatory funnel is allowed to fill with liquid and then the stopcock regulated so that the liquid flows back to the copper vessel as fast as it distils over. A

return tube similar to the one used in the apparatus for the preparation of anhydrous oxalic acid (Fig. 6, p. 68) may be used, but in making methyl hexyl carbinol the separatory funnel has the advantage that if foaming occurs in the reaction flask, further addition of water can be immediately and easily stopped.

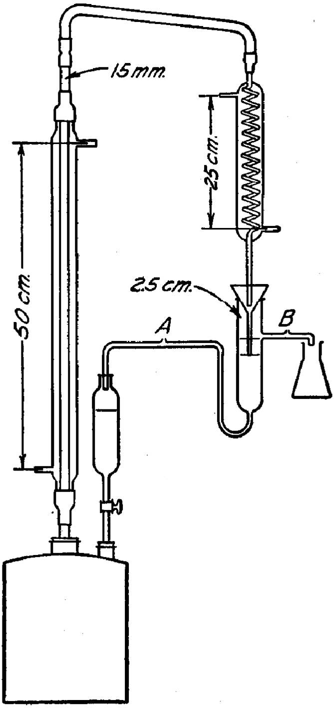



FIG. 5.

The distillation is continued until no more alcohol comes over, a process which requires forty-eight to seventy-two hours of continuous heating. Superheating must be avoided, since foaming will then occur and may cause considerable difficulty. It is therefore advisable to adjust the heating so that the distillate comes over in rapid drops but not in a stream. If cooling

is allowed to take place before the distillation is complete, it is advisable to break up the reaction cake before heating again, or to start the heating at the top of the cake and to approach the bottom gradually. The crude product obtained is very much lighter in color than that produced when cans are used, and when it is distilled only very small fractions of low or high boiling material result. Moreover, the amount of ketones is small. The yields of the redistilled fraction boiling at 175–180° in three successive experiments were 1854 g., 1955 g., and 1894 g. (39–41 per cent theory), quantities about twice those obtained when cans are used. The time that a man actually devotes to the production of methyl hexyl carbinol is not great, but the total time necessary for carrying out a large experiment is almost a week.

## 2. Notes

The best grade of castor oil gives much better results in this experiment than the poorer grades.

The container which is used in the production of methyl hexyl carbinol should not be filled more than half full of reaction mixture, since foaming occurs to a considerable extent during the heating.

The necessity of making holes in the solid soap or heating the top of the soap first, whenever cooling is allowed to take place during the initial heating or distillation is a precaution to which attention should again be drawn.

It is worthy of special note that the yield is much larger when the reaction is carried out in a copper vessel that is capable of being heated to a high temperature without leaking. An iron vessel cannot be substituted for copper. Several runs in iron gave about the same weight of crude product but this always contained high and low fractions that did not appear when copper was used.

Upon adding the water which distils over with the alcohol, to the reaction mixture, the special precaution must be taken of making the addition slowly or else the contact of the cold liquid

with the hot reaction mass causes very bad foaming. If the distillation is too rapid, superheating occurs and excessive foaming is liable to take place. After the methyl hexyl carbinol has all been distilled from the reaction mixture, the residue in the copper vessel should not be allowed to cool directly, as a solid cake that will have to be chiselled out will be formed. After the heating is stopped, it is advisable to add water to the hot residue, very slowly at first, then as the kettle cools, more rapidly. While still fairly hot, however, the mixture is poured into a crock and allowed to cool.

It is probable that stirring during the decomposition of the soap would increase the speed of the reaction and decrease the by-products.

It will be noticed that 5800 g. of water are used in the large runs and then 3000 g. are distilled off and discarded before the alcohol begins to come over rapidly. This quantity of water helps in the formation of the soap, but it is not absolutely necessary; only 2000 or 2500 g. may be used, under which conditions the alcohol begins to come over immediately with the water.

### 3. Other Methods of Preparation

Methyl hexyl carbinol may be made in a pure state by the action of methyl magnesium iodide upon heptaldehyde,[1] but it is more easily and cheaply obtained in a state of satisfactory purity for most purposes by the heating of castor oil with sodium hydroxide.[2] This gives sodium ricinoleate which upon fusion with caustic soda yields methyl hexyl carbinol. Other methods of theoretical interest have also appeared: the product may be prepared by the chlorination and subsequent hydrolysis of petroleum octane;[3] by the distillation of certain rarer oils with sodium hydroxide.[4]

[1] C. A. **11**, 3027 (1917).

[2] C. A. **11**, 3027 (1917); Ann. **87**, 111 (1853); **97**, 34 (1856); **147**, 222 (1868); J. prakt. Chem. **72**, 241 (1857); Ber. **24**, 3351 (1891).

[3] Ann. **152**, 152 (1869).

[4] Z. Chem. **1869**, 185.

## XIV

## OXALIC ACID (ANHYDROUS)

$$(HO)_3CC(OH)_3[H_2C_2O_4 \cdot 2H_2O] \rightarrow HO_2CCO_2H + 2H_2O$$

Prepared by H. T. CLARKE and ANNE W. DAVIS.
Checked by ROGER ADAMS and V. VOORHEES.

### 1. Procedure

IN a 5-l. round-bottom flask are placed 2 kg. of pure crystallized oxalic acid which has been passed through a 10-mesh sieve, and 3 l. of carbon tetrachloride. The flask is then fitted up with a mechanical stirrer and the apparatus shown in Fig. 6 (p. 68). This apparatus consists of an upright water condenser through the jacket of which steam is passed. A connecting tube leads from the top of this condenser to the top of a second efficient spiral condenser, the bottom of which extends into a gravity separator. The water runs off into a receiver and the heavier carbon tetrachloride layer returns to the reaction flask. A few essential points in the apparatus should be mentioned: it is necessary that the return arm of the gravity separator be below the tube through which the water flows into the receiver; the bottom of the funnel should be below the water outlet out as in the diagram; the openings A and B are necessary to prevent siphoning in the respective tubes; the last bend in the return tube before entering the reaction flask serves as a trap to prevent vapors from entering that tube.

The flask is placed up to its neck in hot water, stirring is started and the steam is allowed to flow through the first upright condenser. The heating of the flask and vigorous stirring is continued until no more water passes through into the condenser. This point is indicated by the fact that no more water flows from

the side-arm of the separator. A slight milkiness in the carbon tetrachloride, which persists even when practically no more water comes over, need not be considered. The time of heating depends to a large extent on the rate with which the vapors are

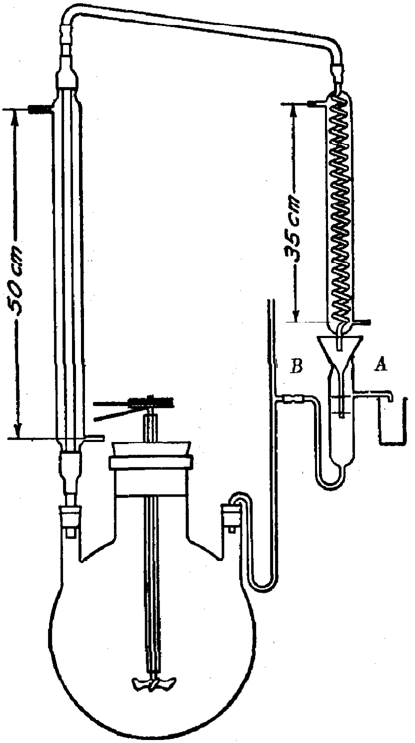



FIG. 6.

distilled over, and this rate in turn depends largely on the efficiency of the condenser. With an ordinary apparatus, such as that described, the time necessary will be approximately eighteen to twenty-four hours. The reaction mixture is now filtered with suction, care being taken that any oxalic acid which

is crusted above the surface of the carbon tetrachloride is not removed with the main portion of the product. The carbon tetrachloride may be used over again for another run, and the anhydrous oxalic acid is dried by short exposure to a warm dry atmosphere. The yield of product amounts to over 90 per cent of the theory.

## 2. Notes

As the time necessary for the dehydration depends almost entirely on the rate of boiling, care must be taken to select an efficient condenser. If a long spiral condenser is not available, a very successful device is to join the top of the upright tube to an ordinary long condenser placed in a slanting position, with its lower end connected by a bent tube of rather large bore to another condenser also in a slanting position, and leading back to the top of the gravity separator, the arrangement being > shape.

The heat may be applied to the flask either by direct flame, water bath, or steam bath.

It is well to place as much liquid in the flask as consistent with rapid boiling, since a slight crust of partially dehydrated acid is apt to collect around the upper edges of the carbon tetrachloride; this stays behind when the anhydrous acid is filtered off, and must not be included in the main product. Complete immersion of the flask in hot water will greatly minimize this trouble, and it is therefore recommended.

Carbon tetrachloride is in every way the most suitable liquid. It is not inflammable; the boiling temperature is such that water is readily evolved but sublimation of anhydrous acid is slight; and as the density is near to that of oxalic acid, an efficient mixing can be obtained. In benzene, the first and third conditions are not fulfilled; in toluene, none of them, for although the water is more rapidly driven off than with carbon tetrachloride the sublimation is so great as to be troublesome, and owing to the less efficient stirring in the liquid of lower density, the acid shows a great tendency to clump.

The stopper should be of good cork, covered if desired with

tin foil. Rubber stoppers are rapidly attacked by the carbon tetrachloride vapors and rendered useless after one run.

The carbon tetrachloride may be used over again in subsequent runs. A considerable portion of carbon tetrachloride is lost in the experiment, and this is the chief disadvantage in the procedure. It is almost impossible to filter the oxalic acid and recover more than about 80 per cent of the carbon tetrachloride. About 18 per cent remains attached to the anhydrous oxalic acid and evaporates when the oxalic acid is dried. The last 2 per cent is lost by evaporation during the dehydration.

### 3. Other Methods of Preparation

Oxalic acid can be dehydrated by heating to about 100° in an oven[1] or in an oil bath at 145–150°[2] but considerable loss occurs through sublimation; this is, moreover, harmful to the oven. This difficulty can be avoided by heating the crystallized acid at about 60° under reduced pressure,[3] removing the evolved water by passing the vapor through a condenser. This method is very slow and it is necessary to interrupt the process at frequent intervals and pulverize the mass which tends to clump and then refuses to lose water. Another method recommended involves treatment with concentrated sulfuric acid;[4] a preliminary trial proved it to be difficult to obtain even a reasonably good yield by this method, while the separation of adhering sulfuric acid offered many difficulties. The method[5] of dehydrating by means of carbon tetrachloride is quite satisfactory for the laboratory.

[1] Bull. soc. chim. (2) **33**, 415 (1880).

[2] Bull. soc. chim. (2) **38**, 406 (1882).

[3] Proc. Chem. Soc. **8**, 186 (1892).

[4] Jahresb. **1864**, 371; Ann. chim. (6) **19**, 58 (1890); Bull. soc. chim. (2) **38**, 406 (1882); Proc. Chem. Soc. **8**, 186 (1892).

[5] J. Am. Chem. Soc. **43**, 366 (1921).

# XV

## THIOPHENOL

$$C_6H_5SO_2Cl+6H(H_2SO_4+Zn) \rightarrow C_6H_5SH+HCl+2H_2O$$

Prepared by ROGER ADAMS and C. S. MARVEL.
Checked by H. T. CLARKE and KATHARINE OGDEN.

### 1. Procedure

IN a 12-l. round-bottom flask are placed 7200 g. of cracked ice and 2400 g. of concentrated sulfuric acid (sp. gr. 1.84). The mixture becomes very cold and is kept at $-5°$ to $0°$ by means of an ice-salt bath. Mechanical stirring is started and 600 g. of crude benzene sulfonyl chloride as prepared in Exp. III (p. 21) are gradually introduced (one-half an hour). Then 1200 g. of zinc dust (90 per cent) are added in portions as rapidly as possible without allowing the temperature to rise above that mentioned (this requires about one-half an hour). The contents of the flask are stirred for one to one and a half hours longer, the temperature being kept at $0°$ or below during the whole period. A stopper holding an efficient reflux condenser (lower end not constricted) and stirrer (Fig. 1, p. 4) is now attached, the ice bath is removed, and the reaction mixture is allowed to warm up spontaneously or it may be warmed up with a low flame, the stirring being continued. Within a very few (two to five) minutes, in many runs, a rather vigorous reaction with the evolution of much hydrogen takes place. Under these circumstances it is advisable to cool the flask momentarily by a stream of water. The reflux condenser will generally take care of the vapors satisfactorily, however. After the first ebullition has subsided, no further attention is required and the mixture is heated to boiling over a ring burner until the solution becomes clear. The stirring should be

continued during the refluxing and the stirrer should be arranged so as to suck the liquid downward from the surface. This helps distribute the zinc which holds hydrogen and floats on top of the liquid. About four to seven hours are required for the heating. The thiophenol is then distilled with steam, this process requiring about one hour. The product is separated from the water, dried with calcium chloride (shaking with calcium chloride for three to five minutes is generally sufficient) and distilled. The crude material weighs 359 g. (96 per cent theory) and the pure substance boiling 166–169° (71° at 15 mm.) 340 g. (91 per cent theory). For the whole experiment up to the final distillation ten to twelve hours are required.

## 2. Notes

The directions given in the literature advise the addition of the zinc dust to the sulfuric acid and then the benzene sulfonyl chloride. This procedure has been reversed in the way described above so that the minimum amount of hydrogen will be lost during the addition of the zinc.

It is essential that the temperature during the first part of the reaction be kept at 0° or below for otherwise poor yields are obtained.

Since benzene sulfonyl chloride solidifies at 15°, it is necessary to add it to the sulfuric acid slowly, with stirring, so that it will be as finely divided as possible when the zinc is added.

In order to hold the temperature at 0°, it is absolutely essential to add the zinc dust at least as slowly as described.

After the initial reaction at a low temperature had taken place, it was, in several instances, found convenient to allow the reaction mixture to stand overnight before proceeding further. The flask was thus left in the ice, which gradually melted allowing the reaction mixture to warm up to room temperature. Under these conditions, however, a poor yield generally resulted. Upon closer study, it was discovered that the small amount of product obtained was due to the sudden vigorous reaction, with consequent loss through the condenser, which took place when a

certain temperature was reached. The reaction mixture may be safely allowed to stand only if a very efficient condenser is used. In the checking of this experiment by Clarke and Ogden, no sudden reaction was observed and heating with a small flame after the initial mixing and stirring at 0°, gave excellent results. The difference in the experiments may have been due to a slightly different grade of raw materials.

Vigorous stirring while the reaction mixture is heated, cuts down materially the time of the reduction (from twelve to seven hours or less), as it brings the zinc which otherwise floats, into intimate contact with the acid and organic sulfur compound.

### 3. Other Methods of Preparation

Thiophenols have been produced by the action of sulfur on benzene in the presence of anhydrous aluminum chloride;[1] by the action of phosphorus pentasulfide on phenol;[2] of zinc on a mixture of sulfur chloride and benzene;[3] of sulfur chloride on benzene in the presence of anhydrous aluminum chloride;[4] by the fusion of the sodium salt of benzene sulfonic acid and sodium sulfhydrate;[5] by the dry distillation of the sodium salt of benzene sulfonic acid.[6] These methods, however, in every case give impure products and in very small yields so that no study was made of them. There are two methods described which do give satisfactory results for thiophenols. The first is by the treatment of aryl diazonium chlorides with potassium ethyl xanthogenate to give aryl ethyl xanthogenates; these compounds upon heating with alkali give thiophenols.[7] The reaction is very general and by it a large number of thiophenols have been prepared. Many side reactions may take place, how-

[1] Ann. chim. (6) **14**, 437 (1888).
[2] Z. Chem. **3**, 194 (1867).
[3] Ber. **11**, 1173 (1878).
[4] Ann. chim. (6) **1**, 531 (1884).
[5] Ber. **17**, 2080 (1884).
[6] Ann. **149**, 248 (1869).
[7] D. R. P. 45,120; Winther Patente der Organischen Chemie **I**, 243; J. prakt. Chem. (2) **41**, 179 (1890); Gazz. chim. ital. **21**, I, 213 (1891).

ever, and care is necessary in the preparation; it is reported[1] that in a number of instances violent explosions occurred when the conditions were not correct. The method is certainly not as simple to carry out as the reduction of sulfonyl chlorides. It does not give as good yields nor as pure products as the latter method; moreover, extraction with ether and treatment with alcoholic potassium hydroxide are both necessary. The second satisfactory method is the reduction of sulfonyl chlorides by means of zinc dust and sulfuric acid,[2] as described by R. Otto and E. Bourgeois. It can be seen immediately that this method is not applicable to any compound which may contain groups likely to be reduced with zinc and sulfuric acid, as for example a nitro compound, and thus it is more limited in its use than the diazonium reaction. For many of the simpler thiophenols, however, such as thiophenol itself and thiocresol, the results are very satisfactory, since the raw materials are easy to make and clean products in good yields are easily obtained. This procedure in this case is preferable to the preparation through the amines.

[1] Ber. **28**, 3240 (1895).

[2] Ann. **119**, 142 (1861); Ber. **10**, 939 (1877); especially Ber. **28**, 2319 (1895); Rec. trav. chim. **18**, 433 (1899); Ber. **51**, 751 (1918).

# XVI

## TRIMETHYLAMINE

$$3(CH_2O)_3 + 2NH_4Cl \rightarrow 2(CH_3)_3N \cdot HCl + 3CO_2 + 3H_2O$$
$$(CH_3)_3N \cdot HCl + NaOH \rightarrow (CH_3)_3N + NaCl + H_2O$$

Prepared by ROGER ADAMS and B. K. BROWN.
Checked by J. B. CONANT and A. McB. KINNEY.

### 1. Procedure

FIVE HUNDRED grams of technical ammonium chloride (2 moles) and 1330 g. of paraformaldehyde (corresponding to 9 moles of formaldehyde) are mixed together and allowed to react as described under Exp. XVII "Trimethylamine Hydrochloride" (p. 79). To obtain from this crude reaction-mixture a water or alcohol solution of trimethylamine, it is not satisfactory merely to treat with alkali and lead the trimethylamine through the solvent, since the gas is inefficiently absorbed; in fact, it is almost impossible to get a concentrated solution in this way without loss of material. The best way to prepare a solution is to liquefy the trimethylamine (b. p. 3.5°) and in this form run it into the solvent. For this purpose, the 5-l. flask in which the initial reaction is carried out is fitted with a rubber stopper holding a separatory funnel and a glass tube for leading off the trimethylamine. This tube is run into one opening of a large U tube or Wolff bottle holding soda lime for drying the gas. The exit tube from this drying bottle has a glass tube leading to the top of an upright condenser which consists of a spiral tube cooled with a freezing mixture (Fig. 7, p. 76, see also Notes). The bottom of this condenser leads through a rubber stopper fitting tightly in a 2- or 3-l. flask, holding the solvent and im-

mersed in an ice-salt mixture. An exit tube from this flask leads to a Wolff bottle kept at a low temperature and holding a little solvent, and through this solvent any unabsorbed trimethylamine must bubble. The exit tube of this last Wolff bottle is closed with a soda lime tube if an anhydrous solvent is being used.

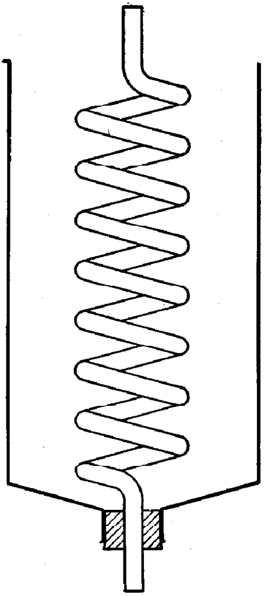


FIG. 7.

The separatory funnel is filled with sodium hydroxide solution (1100 g. in 2000 cc. of water) which is then allowed to flow into the reaction mixture at such a speed that after the air in the apparatus has been replaced by trimethylamine, a continuous stream of drops of trimethylamine flows from the condenser into the solvent and practically no gas goes through the end Wolff bottle. At the beginning, the evolution of trimethylamine is rapid and hence the addition of the alkali must be very slow; as soon as the reaction mixture is partly decomposed,

however, the alkali may be added more rapidly. After it has all been added, the reaction mixture is heated ten to fifteen minutes to make sure that all of the amine is evolved. The time for this alkali treatment is about three to four hours.

With such an experiment as is described above, using 1000 g. of absolute alcohol in the solvent flask and about 150 g. in the end Wolff bottle, 1469 g. of solution are obtained in the main flask and 174 g. in the Wolff bottle, thus indicating that a total of 491 g. (89 per cent theory) of trimethylamine are present. There is thus obtained a 32 per cent solution in the main flask which has a sp. gr. of about 0.760 at $+5°$. By titration with standard hydrochloric acid, the same amounts of trimethylamine are indicated, as are found by weighing. In several experiments, the yields were consistently 85–90 per cent of the theory.

## 2. Notes

As trimethylamine is very volatile and easily lost, particular care must be taken to have all connections in the apparatus tight.

If water is to be used as a solvent, no soda lime tube is necessary on the exit of the end Wolff bottle. Moreover, with water as a solvent it is not absolutely necessary to have the soda-lime tube between the generating flask and the solvent. It is advisable to have it there, however, since it tends to catch any small amount of colored liquid coming from the reaction flask and thus prevents contamination of the water solution obtained.

During the evolution of the trimethylamine, it is necessary occasionally to shake the flask containing the solvent. It happens that after about a 10–15 per cent solution is formed, the trimethylamine tends to form a top layer which is not dissolved until agitated.

Titration of the strength of the trimethylamine in the solvent is best done by pipetting out 1 cc. of the solution and allowing it to run immediately into 50 cc. of water. This is to prevent volatilization during titration. The amine is then titrated in the usual way with standard hydrochloric acid, using methyl orange as an indicator.

In order to avoid loss of material, the sp. gr. of any trimethylamine solution must be taken at a low temperature. In this experiment, $+5^\circ$ was chosen.

Since tests in the following experiment indicate that only trimethylamine is formed in this reaction, it is unnecessary to purify the trimethylamine solution.

Special attention should be drawn to the condenser (Fig. 7, p. 76) used since it is valuable in many other experiments wherever substances having a boiling-point between $-10^\circ$ and $+30^\circ$ are being handled. Any gallon can, having an opening in the top in which a stopper may be inserted, is satisfactory for a jacket. The bottom of the can is cut out and the can is then inverted. A spiral tube such as that which may be obtained from the inside of a spiral condenser is placed in the can with the lower end fitting tightly through the stopper in the neck. By filling the can with an ice and salt mixture a condensing temperature of $-10^\circ$ or below can easily be obtained.

### 3. Other Methods of Preparation

The references to the preparation of trimethylamine are referred to in the following experiment entitled "Trimethylamine Hydrochloride."

## XVII

# TRIMETHYLAMINE HYDROCHLORIDE

$$3(CH_2O)_3 + 2NH_4Cl \rightarrow 2(CH_3)_3N \cdot HCl + 3CO_2 + 3H_2O$$

Prepared by Roger Adams and C. S. Marvel.
Checked by J. B. Conant and A. McB. Kinney.

## 1. Procedure

Five hundred grams of technical ammonium chloride (2 moles) and 1330 g. of paraformaldehyde (corresponding to a fraction over 9 moles of formaldehyde) are thoroughly mixed and placed in a 5-l. round-bottom flask fitted with a long reflux condenser (a jacket of about 100 cm. length and an inner tube of about 2 cm. diameter). By means of an oil bath, the temperature of the reaction mixture is gradually raised. Between 85° and 105° liquefaction at the bottom of the flask begins to take place and at the same time a very vigorous evolution of carbon dioxide starts. The heat is at once withdrawn and if the reaction is too violent, the oil bath should be removed. The reaction is allowed to continue without further heating until the gas evolution is less vigorous. This requires about one and a half hours. Heat is again applied and the temperature of the bath raised to about 160°, where it is held until there is practically no more evolution of carbon dioxide. This takes two and a half to three and a half hours, after which time the reaction is complete. To obtain the trimethylamine hydrochloride, it is now merely necessary to treat the mixture with sodium hydroxide, and to distil the free amine into hydrochloric acid. A separatory funnel is therefore inserted through the stopper of the flask and the reflux condenser is changed to a downward position for distillation. The open end of the condenser is fitted tightly into the neck of a boiling flask or suction flask, to the outside arm of

which is attached by means of rubber tubing, a glass tube which leads under hydrochloric acid in a receiver. Care must be taken to have all the joints in the apparatus tight as the trimethylamine is very volatile and can easily be lost. The object of the intermediate boiling or suction flask is to catch any water which may distil with the trimethylamine during the treatment with the sodium hydroxide. This water is often colored yellow, and if allowed to go directly into the hydrochloric acid in the receiver contaminates the trimethylamine hydrochloride. A solution of 1100 g. of sodium hydroxide (two and a half to three times the amount theoretically necessary to liberate the free amine) in 2000 cc. of water is allowed to drop through the separatory funnel into the reaction mixture, which has cooled somewhat during the change of apparatus. The amine distils, passes through the condenser, through the intermediate bottle and into the receiver, in which is placed an amount of concentrated hydrochloric acid (930 cc. of sp. gr. 1.19) slightly more than enough to neutralize the weight of amine which should theoretically be formed. To be certain that all the amine has been driven from the reaction flask, heat is finally applied for ten or fifteen minutes to the mixture. The whole procedure from the beginning of the first reaction until a solution of trimethylamine hydrochloride is obtained, requires not more than six to seven hours.

To obtain the trimethylamine hydrochloride, the hydrochloric acid solution is evaporated, first over a free flame and later, when the crystals start to form, on a steam bath. As the solution gets more and more concentrated, the trimethylamine hydrochloride crystallizes out and is filtered from time to time, is dried for a few minutes in an air bath, temperature 100–110°, and is finally kept in a tightly closed bottle. If the trimethylamine hydrochloride as it crystallizes is centrifuged, the product is obtained pure and dry at once. The average yield from four runs is 710 g. of perfectly pure trimethylamine hydrochloride and 82 g. of product which is tinged slightly yellow (a total of 89 per cent theory based on the ammonium chloride). This coloration results from the evaporation to dryness of the very last portion of solution.

## 2. Notes

The reaction takes place with the evolution of a considerable amount of heat and consequently a condenser as efficient as that mentioned is necessary in order to avoid loss. The wide inner tube is used to avoid any possibility of paraformaldehyde subliming and plugging the condenser.

The complete solubility of the product in chloroform [1] shows the trimethylamine hydrochloride to be free from ammonium chloride and methylamine hydrochloride and the fact that no precipitate is obtained when tested with sodium hydroxide and benzene sulfonyl chloride in aqueous solution shows that dimethylamine hydrochloride is absent.

## 3. Other Methods of Preparation

It is reported that trimethylamine in combination occurs in large amounts in beet-root residues [2] and can be obtained from them by the action of caustic soda; it occurs also in herring brine.[3] From both of these sources, however, the substance is obtained in an impure state and can be purified only by rather tedious methods. This is indicated by the fact that trimethylamine has always been an expensive substance. Synthetic methods for its production are by the action of methyl iodide on ammonia; [4] by the distillation of tetramethylammonium hydroxide; [5] by the action of magnesium nitride upon methyl alcohol; [6] by the action of zinc upon trimethyloxyammonium halides; [7] by the action of formaldehyde upon ammonium chloride under pressure; [8] by the action of ammonium chloride upon paraformaldehyde.[9] Of these syn-

[1] Compt. rend. **150**, 1251 (1910).
[2] Bull. soc. chim. (1) **27**, 150 (1877); Ber. **13**, 1669 (1880).
[3] Ann. **93**, 321 (1855).
[4] Ann. **79**, 16 (1851).
[5] Ann. **267**, 263 (1892).
[6] Ber. **30**, 306 (1897).
[7] Ber. **31**, 2064 (1898).
[8] Ber. **38**, 882 (1905); Bull. soc. chim. (3) **13**, 536 (1895).
[9] D. R. P. 270,260; Frdl. **11**, 111 (1912–14).

thetic methods the only ones which are cheap enough for the production of trimethylamine in large amounts are the last two. The action of ammonium chloride upon formaldehyde, however, must be carried out in autoclaves and at best only very small amounts of trimethylamine can be prepared in a reasonable time. The paraformaldehyde-ammonium chloride method developed by R. H. Schmitz runs very smoothly and gives an exceptionally pure product. This method, was, therefore, the only one investigated.

Since the appearance of Vol. I of Organic Syntheses, a new method described by Sommelet and Farrand by allowing ammonia, formaldehyde and formic acid to react has appeared in the literature.[1] The method has been checked by one of the editors and is highly recommended.

Other literature references may be found in Org. Syn. **6**, 108.

[1] Bull. soc. chim. (4) **35**, 446 (1924).

# INDEX

# ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS



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VOL. II.

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# INTRODUCTION TO THE SERIES

THE publication of this series of pamphlets has been undertaken to make available in a permanent form complete detailed directions for the preparation of various organic chemical reagents. In announcing this purpose it may be well to mention at the outset some of the difficulties in the way of the research chemist, which it is hoped this series will be able to overcome. The cost of chemicals is prohibitive to the majority of chemists; this was true before the war when Kahlbaum's complete supply was available, and to-day with our dependence on domestic stocks, this cost has increased. The delay in obtaining chemicals, especially from abroad, even if the expense need not be considered, is an important factor. These difficulties have therefore thrown the research chemist on his own resources. The preparation of materials for research, always time consuming and annoying, is made increasingly so by the inexactness of the published information which so often omits essential details. Because of this, much needless experimentation is necessary in order to obtain the results given in the published reports. As the additional information thus acquired is seldom published, duplication of such experiments occurs again and again,—a waste of time and material. It is hoped these difficulties may be remedied by the publication of this series of pamphlets. In other words, the authors hope to make this a clearing house for the exchange of information as to methods of preparation of some of the most needed organic chemical reagents.

On account of the impossibility of obtaining the less common organic chemicals in the United States during the past few years,

university laboratories have had no option but to prepare their own supplies. At the University of Illinois, for instance, a special study has been made of this field, and methods for the production of various substances have been investigated. As a result, reliable methods and directions have been developed for producing the materials in one-half to five pound lots. Such work as Illinois has done is now being given an even more extensive scope at the Research Laboratory of the Eastman Kodak Company. It is felt that the results from these various laboratories should be available to all chemists and it is hoped that they eventually will be completely incorporated in these pamphlets.

The organic chemicals herein discussed have been quite arbitrarily chosen, being those which have been needed in various research laboratories in the last years and for which the directions happen now to be ready for publication. The methods are in only a few cases new ones; they are in general the most satisfactory to be found in the literature. Only such details have been added as will enable a man with a reasonable amount of experience in organic chemistry to duplicate the results without difficulty. To be absolutely sure that each set of directions can be repeated, every experiment has been carried out in at least two laboratories. Only after exact duplication of the results in both laboratories are the directions considered ready for publication. The names of the chemists who have studied the various experiments are given so that further information concerning any obscure point can be obtained if any question arises in using these directions. And finally, in describing the experiments, special attention has been given to the explanation of why it is necessary to follow the directions carefully, and what will happen if these directions are not followed.

Although the main object in this series is to give the most convenient laboratory methods for preparing various substances in one-half to five pound lots, an attempt has also been made to have these processes as far as possible adaptable to large scale development. For example, extractions have been avoided wherever possible, cheap solvents have been sub-

stituted for expensive ones, and mechanical agitation, a procedure extremely important in the success of many commercial processes, has usually been specified. The apparatus used is always carefully described and wherever necessary an illustration is given. Accompanying each preparation there will be found a bibliography containing references to all the methods for the production of the substance described in the literature. This is given in order to aid any future investigator who may wish to study or improve the methods of preparation. It is not claimed that the methods are, in every case, completely perfect, but only that the yields are very satisfactory and allow the production of the substances at a reasonable cost. It is hoped therefore that the pamphlets will benefit not only the scientific research man of the university, but also the technical chemist who desires to develop the preparation of one of these substances to a large scale process of manufacture. The editors trust also that this work may be used to advantage as a preparation manual in intermediate or advanced courses in organic chemistry in university laboratories, and that it will aid small colleges in the production of necessary reagents which they are often financially unable to purchase.

The pamphlets are to be edited by the following committee: Roger Adams, University of Illinois, Urbana, Illinois; J. B. Conant, Harvard University, Cambridge, Massachusetts; H. T. Clarke, Eastman Kodak Company, Rochester, New York; Oliver Kamm, Parke, Davis Company, Detroit, Michigan; each to act for one year as editor-in-chief and the other three to assist him as associate editors. A new number of the series will appear annually, and every five years the data will be rearranged, revised, corrected, and then published in book form. The number of preparations to be completed yearly is not fixed. There will be, it is certain, about twenty; and it is hoped, as the interest is stimulated in this work, that this number may increase considerably. The editors especially desire to solicit contributions from other chemists, not only in this country but abroad. Whenever a compound is thoroughly and extensively studied in connection with some research, it is hoped that

complete directions for its preparation will be assembled and sent to the editor. He will then have them checked and published in a subsequent number. Directions for the preparation of substances already on the market are needed to make this work complete and will be gladly accepted.

It will, of course, be recognized that an occasional mistake or omission will inevitably be found in such a pamphlet as this which contains so many references and formulæ. The committee on publication will therefore deem it a favor if they are notified when any such error is discovered. It is hoped also that if any chemist knows a better method for the preparation of any of the compounds considered, or if anyone discovers any improvements in the methods, he will furnish the authors with such information. Any points which may arise in regard to the various preparations will be gladly discussed. In conclusion, the editors are ready to do all they can to make this work successful, and welcome suggestions of any kind. They feel that the success of the series will undoubtedly depend upon the cooperation of others, and as its success promises to be important to research chemists, the editors urge all interested to assist.

THE EDITORS

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## I

### BENZALACETOPHENONE

$$C_6H_5CHO + C_6H_5COCH_3 + (NaOH) \rightarrow C_6H_5CH{=}CHCOC_6H_5 + H_2O$$

Prepared by E. P. Kohler and H. M. Chadwell.
Checked by H. T. Clarke and R. P. Leavitt.

#### 1. Procedure

A solution of 218 g. of sodium hydroxide in 1960 g. of water and 1000 g. of 95 per cent alcohol are introduced into a 5500-cc. bottle which is loosely covered with a perforated disk of cardboard, supplied with an effective stirrer, and supported in a larger vessel so as to permit cooling with cracked ice. Into the alkaline solution, 520 g. of pure acetophenone is poured, the bottle is rapidly surrounded with cracked ice, and the stirrer started; 460 g. of benzaldehyde (U. S. P.) are then added at once. The temperature of the mixture should not be below 15° and it should not be allowed to rise above 30° during the reaction. If it tends to do so, the stirring is not sufficiently vigorous.

It is advantageous, though not essential, to inoculate the mixture with a little powdered benzalacetophenone after stirring for half an hour. After two to three hours, the mixture becomes so thick that the stirring is no longer effective. The stirrer is then removed and the mixture left to itself in an ice-box for about ten hours. The mixture now is a thick paste composed of

small shot-like grains suspended in an almost colorless liquid. It is cooled in a freezing mixture and then either centrifuged or filtered on a large Buchner funnel, washed with water until the washings are neutral to litmus, and finally washed with 200 cc. of alcohol, which has previously been cooled to 0°. After thorough drying in the air, the crude product weighs about 880 g. (yield 97 per cent of the theoretical amount) and melts at 50–54°. It is sufficiently pure for most purposes but tenaciously holds traces of water. It is most readily purified by recrystallization from four to four and a half times its weight of 95 per cent alcohol. Eight hundred and eighty grams of crude product give 770 g. (85 per cent of the theoretical amount) of light-yellow material (m. p. 55–57°) and 40–50 g. that require recrystallization.

## 2. Notes

The acetophenone should be as pure as possible (m. p. 20°). Commercial acetophenone contains variable quantities of impurities which reduce the yield. By distilling commercial acetophenone with the help of a good still-head (preferably under diminished pressure) and using only the fraction which boils at 201–202° (76–77°/10 mm.) greater quantities of benzalacetophenone can be obtained than by using the entire sample.

Commercial benzaldehyde can be used in place of the purer product, but the amount used must be increased to make up for the impurities which are present.

If the temperature is too low, or the stirring too slow, the product separates as an oil, which later solidifies in large lumps.

If the temperature is allowed to rise above 30°, secondary reactions diminish both the yield and the purity of the product. The most favorable temperature is 25°.

In recrystallizing benzalacetophenone, the alcohol should be saturated at 50°. If the solution is saturated above this temperature, the benzalacetophenone tends to separate as an oil. The solution should be allowed to cool gradually, and should finally be chilled in a freezing mixture.

### 3. Other Methods of Preparation

The methods for producing benzalacetophenone are: the action of acids on a mixture of benzaldehyde and acetophenone or on a solution of these substances in glacial acetic acid;[1] the condensation of benzaldehyde and acetophenone with a 30 per cent solution of sodium methylate at low temperatures;[2] the action of sodium hydroxide on an alcoholic solution of benzaldehyde and acetophenone.[3]

The methods based on the use of acids as condensing agents were not considered, because Claisen, who devised them, abandoned them after he found that alkaline condensing agents gave better results. The preliminary experiments showed that condensation with sodium methylate takes a long time and gives a product which it is difficult to handle in large quantities. The method devised by Kostanecki and Rossbach[3] has therefore been developed.

[1] Ber. **14**, 2463 (1881).
[2] Ber. **20**, 657 (1887).
[3] Ber. **29**, 1492 (1896).

## II

## BENZYL BENZOATE

$$2\ C_6H_5CHO + C_6H_5CH_2ONa \rightarrow$$

$$C_6H_5CO_2CH_2C_6H_5 + C_6H_5CH_2ONa$$

Prepared by O. Kamm and W. F. Kamm.
Checked by Roger Adams and R. L. Jenkins.

### 1. Procedure

Three grams of metallic sodium are dissolved by warming for half an hour in 70 g. of pure benzyl alcohol (see notes), and after the mixture has cooled to room temperature the solution is added gradually, with thorough mixing, to 454 g. of c. p. benzaldehyde (which must contain *less* than 1 per cent of benzoic acid). The reaction mixture has a tendency to become warm, but the temperature should be kept slightly below 50–60° by cooling, if necessary. A pasty gelatinous mass results. After about half an hour the temperature of the mixture no longer rises; it is then warmed on the water bath for about one or two hours, with occasional shaking.

The cooled reaction product is treated with 200 cc. of water, the layer of oil separated, washed once with a second portion of water, and subjected to distillation *in vacuo*. The first fraction of the distillate contains benzyl alcohol together with unchanged aldehyde, as well as a small quantity of water. The temperature then rises rapidly to the boiling-point of benzyl benzoate, when the receivers are changed. The product boils at 184–185°/15 mm., and analysis by saponification shows it to consist of 99 per cent ester. A yield of 410–420 g. is obtained, which corresponds to 90–93 per cent of the theoretical amount. This benzyl benzoate supercools readily, but after solidifying

melts within one degree of the highest recorded value (19.4°) and therefore need not be refractionated, unless material of exceptional grade is required.

## 2. Notes

In the presence of sodium benzylate two molecules of benzaldehyde react with the alcoholate to form an addition product. When the reaction mixture is overheated an important side reaction may occur, as follows:

$$C_6H_5C\begin{cases}OCH_2C_6H_5\\OCH_2C_6H_5\\ONa\end{cases} \rightarrow C_6H_5CO_2Na + C_6H_5CH_2OCH_2C_6H_5$$

Dibenzyl ether no doubt forms the chief impurity in benzyl benzoate. Since the boiling-point of the former lies near that of the ester, it is not removed during the process of purification by distillation.

The causes of variations in yield by the use of the older methods can now be explained. When benzaldehyde is added *to the alcoholate*, and especially when the latter is still warm, local overheating results; in fact, the temperature may rise far above 100° with the result that benzyl ether is formed. Simultaneously, the sodium benzylate is converted into sodium benzoate, which is of no value for inducing the desired reaction, and consequently very little benzyl benzoate is obtained. The same side reactions explain the failure of this experiment when the benzyl alcohol used in preparing the catalyst (sodium benzylate) is contaminated with benzaldehyde.

The benzyl alcohol used in this preparation must be free from impurities, especially aldehyde. One cc. dissolved in 50 cc. of water and treated with a freshly prepared clear solution of phenylhydrazine acetate should give no appreciable precipitate. If it is not pure, it must first be treated with alkali as described below.

The benzaldehyde should be titrated in order to determine its acidity. If it is found to contain sufficient benzoic acid to react with a considerable proportion of the sodium alcoholate,

a poor yield of ester will be obtained. Less than 1 per cent of benzoic acid will not interfere seriously with the yields obtained, but the presence of larger quantities of acid will be found to be detrimental and must be removed by washing the benzaldehyde with a sodium carbonate solution and redistilling with the precautions necessary to prevent too free an access of air to the distillate.

The order of mixing the reagents and the temperature of the ingredients at the time of mixing are the most important factors in the experiment. The temperature at which the reaction mixture is maintained after mixing, provided that it is held below 100°, is less important from the standpoint of purity.

The reaction mixture is not treated with acetic acid, as usually recommended, for the reason that such a procedure yields a final product contaminated with benzoic acid, unless an alkaline wash is applied subsequently.

The recovered benzyl alcohol can be used for the preparation of a second lot of benzyl benzoate only after it has been boiled with strong sodium hydroxide to remove all traces of benzaldehyde.

### 3. Other Methods of Preparation

Benzyl benzoate has been identified in certain natural plant products.[1] In the laboratory it has been prepared by the action of (*a*) benzoyl chloride upon benzyl alcohol,[2] (*b*) benzyl chloride upon sodium benzoate, and (*c*) alcoholates upon benzaldehyde.[3] Recently, Gomberg and Buchler[4] have shown that reaction (*b*) may be conducted even with aqueous solutions of sodium benzoate.

The Claisen method (*c*) furnishes the most convenient and practical procedure for the preparation of this ester. The materials are cheap, the experimental procedure simple, and the product obtained is free from objectionable traces of benzyl

[1] Ann. **152**, 131 (1869).
[2] Gmelin's Handbuch der Organ. Chem. **3**, 40.
[3] Ber. **20**, 649 (1887). Cf. also J. Chem. Soc. **75**, 1155 (1899).
[4] J. Am. Chem. Soc. **42**, 2059 (1920).

chloride. Unfortunately, the method has been found to be extremely erratic in regard to yield (10-95 per cent), as well as in regard to purity of the product (87-97 per cent ester).[1] As a result of the present study,[2] causes for variations are fully accounted for and the procedure has been converted into a satisfactory method of preparation.

[1] C. A. **14**, 3500 (1920).

[2] J. Am. Pharm. Assoc. **11**, 599 (1922).

# BENZYL CYANIDE

$$C_6H_5CH_2Cl+NaCN \rightarrow C_6H_5CH_2CN+NaCl$$

Prepared by Roger Adams and A. F. Thal.
Checked by O. Kamm and A. O. Matthews.

## 1. Procedure

In a 5-l. round-bottom flask, fitted with a stopper holding a reflux condenser and separatory funnel, are placed 500 g. of powdered sodium cyanide (96–98 per cent pure) and 450 cc. of water. The mixture is warmed on a water bath in order to dissolve most of the sodium cyanide, and then 1 kg. of benzyl chloride (b. p. 170–180°) mixed with 1 kg. of alcohol is run in through the separatory funnel in the course of one-half to three-quarters of an hour. The mixture is then heated with a reflux condenser on the steam bath for four hours, cooled and filtered with suction to remove most of the sodium chloride. It is well to wash the filtered salt with a small portion of alcohol in order to remove any benzyl cyanide which may have been mechanically held. The flask is now fitted with a condenser, and as much alcohol as possible is distilled off on the steam bath. The residual liquid is cooled, filtered if necessary, and the layer of benzyl cyanide separated. This crude benzyl cyanide is now placed in a Claisen distilling flask and distilled *in vacuo*, the water and alcohol coming over first, and finally the cyanide. It is advantageous to use a fractionating column or, better still, a Claisen flask with a modified side-arm[1] (Vol. 1, p. 40, Fig. 3) which gives the same effect as a fractionating column. The material is collected from 135–140°/38 mm. (115–120°/10 mm.). The yield is 740–830 g. (80–90 per cent of the theoretical amount).

[1] J. Am. Chem. Soc. **39**, 2718 (1917).

## 2. Notes

The quality of the benzyl chloride markedly affects the yield of pure benzyl cyanide. If a poor technical grade is used, the yields will not be more than 60–75 per cent of the theoretical, whereas consistent results of about 85 per cent or more were always obtained when a product was used that boiled over 10°. The technical benzyl chloride at hand yielded on distillation about 8 per cent of high-boiling material; a technical grade from another source was of unusual purity and boiled over a 2° range for the most part.

It is advisable to distil off the last portion of alcohol and water *in vacuo* and also to distil the benzyl cyanide *in vacuo*, since under ordinary pressures a white solid invariably separates during the distillation.

One method of purifying the benzyl cyanide is to steam distil it after the alcohol has been first distilled from the reaction mixture. At ordinary pressures, this steam distillation is very slow and, with an ordinary condenser, requires eighteen to twenty hours in order to remove all of the volatile product from a run of 500 g. of benzyl chloride. The distillate separates into two layers; the benzyl cyanide layer is removed and distilled. The product obtained in this way is very pure and contains no tarry material, and, after the excess of benzyl chloride has been removed, boils practically constant. This steam distillation is hardly advisable in the laboratory.

The benzyl cyanide, prepared according to the procedure as outlined, is collected over a 5° range. It varies in appearance from a colorless to a straw-colored liquid and often develops appreciable color upon standing. For a product of special purity, it should be redistilled under diminished pressure and collected over a 1–2° range. For most purposes, such as the preparation of phenylacetic acid or ester, the fraction boiling 135–140°/38 mm. is perfectly satisfactory.

### 3. Other Methods of Preparation

Benzyl cyanide occurs naturally in certain oils.[1] The only feasible method of preparing it that has been described in the literature is the one in which alcoholic potassium cyanide and benzyl chloride[2] are employed. The cheaper sodium cyanide is just as satisfactory as the potassium cyanide and therefore is the best material to use. Gomberg has recently prepared benzyl cyanide from benzyl chloride and an aqueous solution of sodium cyanide.[3]

[1] Ber. **7**, 519, 1203 (1874); **32**, 2337 (1899).
[2] Ann. **96**, 247 (1855); Ber. **3**, 198 (1870); **14**, 1645 (1881); **19**, 1950 (1886).
[3] J. Am. Chem. Soc. **42**, 2059 (1920).

IV

## α, γ-DICHLOROACETONE

$$CH_2ClCHOHCH_2Cl + O(Na_2Cr_2O_7 + H_2SO_4) \rightarrow CH_2ClCOCH_2Cl + H_2O$$

Prepared by J. B. Conant and O. R. Quayle.
Checked by A. W. Dox, L. Yoder, and O. Kamm.

### 1. Procedure

In a 2-l. flask are placed 375 g. of commercial sodium dichromate, 225 cc. of water, and 300 g. of dichlorohydrin (b. p. 68–75°/14 mm.). The flask is set in a water bath and equipped with a thermometer and mechanical stirrer. The contents are vigorously stirred, and 450 g. of sulfuric acid, diluted with 115 g. of water, are introduced during the course of seven to eight hours. It is convenient to add the acid at ten-minute intervals. The temperature is kept between 20° and 25° during the entire reaction; this is accomplished by adding a little ice to the water bath from time to time. The stirring is continued for sixteen to seventeen hours after all the acid has been added; as there is very little heat evolved during this part of the reaction, the water bath may be allowed to come to room temperature.

Sufficient water is now added to the mixture to dissolve the pasty chromium salts (300–800 cc.). The mass of crystals is then rapidly filtered on a Buchner funnel and sucked as dry as possible. The crystals are then transferred to a small laboratory centrifuge and centrifuged for several minutes. The crystals are washed in the centrifuge with about 15–25 cc. of ice water, then with 10–15 cc. of cold petroleum ether, and finally centrifuged till as dry as possible. The crude dichloroacetone is dried in a vacuum desiccator over sulfuric acid overnight. It weighs about 220 g.

The crude product is best purified by distillation from a 250-cc. distilling flask fitted with an air condenser. A very small fraction (10–15 g.) of low-boiling material is obtained, and the dichloroacetone (170–175°) is then collected. It solidifies in the receiver to a white crystalline mass which weighs 200–220 g. (65–70 per cent of the theoretical amount). A few grams more may be obtained by chilling the low-boiling fraction and filtering off the water.

## 2. Notes

Great caution should be exercised in working with dichloroacetone, as it is extremely lachrymatory and blisters the skin.

In transferring the crystals from the reaction flask to the Buchner funnel it is necessary to use a certain amount of water to dissolve the pasty chromium salts which are otherwise quite impossible to filter. The amount necessary varies greatly in different runs, according to the manner in which the chromium salts separate. The amount of this water is kept low in order to dissolve as little of the product as possible. Nevertheless, 10–15 g. of dichloroacetone are thus dissolved; this material, together with a little unchanged dichlorohydrin, may be recovered by a long procedure involving extraction with ether and sodium bisulfite. This is not profitable, however.

It is not necessary to wash the crystals in the centrifuge until they are white. A small amount of chromic salt will not interfere with the subsequent purification.

Commercial sodium dichromate is hygroscopic and contains varying amounts of water. The 375 g. required in these directions are equivalent to 319 g. of anhydrous material.

The total time required for the oxidation is twenty-four hours. It is convenient to start the reaction in the morning. In this way the last part of the reaction, which requires no attention, will be accomplished during the night. The regulation of the temperature is necessary, as the reaction proceeds very slowly below 20°; on the other hand, the dichloroacetone itself is oxidized at a somewhat higher temperature than 25°.

## 3. Other Methods of Preparation

The preparation of dichloroacetone by the following methods is described in the literature: the direct chlorination of acetone;[1] the oxidation of dichlorohydrin;[2] the action of silver chloride on diiodoacetone;[3] the action of dichloropropene ($CH_2Cl-CCl=CH_2$) and hypochlorous acid;[4] the action of hydrochloric acid on ethoxymonochloroacetoacetic ester;[5] and the hydrolytic cleavage of dichloroacetoacetic ester.[6]

[1] Jahresb. **1859**, 345; **1871**, 531; J. prakt. Chem. (2) **4**, 52 (1871); Ber. **7**, 467 (1874); **8**, 1330, 1438 (1875); **26**, 598 (1893); **42**, 3233 (1909); Ann. **279**, 315 (1894).

[2] Ber. **6**, 1210 (1873); **13**, 1706 (1880); **42**, 3233 (1909); Ann. **208**, 355 (1881); **269**, 46 (1892); Ann. chim. phys. (6) **9**, 145 (1886); Bull. soc. chim. (2) **36**, 19 (1881).

[3] Ann. **192**, 93 (1878).

[4] Compt. rend. **94**, 1428 (1882).

[5] Ann. **269**, 18 (1892).

[6] Ber. **43**, 3533 (1910).

# V

## p-DIMETHYLAMINOBENZALDEHYDE

$$(CH_3)_2NC_6H_5 + HNO_2 \rightarrow (CH_3)_2NC_6H_4NO + H_2O$$

$$(CH_3)_2NC_6H_4NO + 2\ HCHO + 2\ C_6H_5N(CH_3)_2 \rightarrow (CH_3)_2NC_6H_4N = CHC_6H_4N(CH_3)_2 + 2\ H_2O + (CH_3)_2NC_6H_4CHO$$

$$(CH_3)_2NC_6H_4N = CHC_6H_4N(CH_3)_2 + HCHO \rightarrow (CH_3)_2NC_6H_4N = CH_2 + (CH_3)_2NC_6H_4CHO$$

Prepared by ROGER ADAMS and G. H. COLEMAN.
Checked by H. T. CLARKE and W. W. HARTMAN.

### 1. Procedure

IN a 3-l. round-bottom flask fitted with a mechanical stirrer 150 g. of technical dimethylaniline are dissolved in 750 cc. of diluted hydrochloric acid (1 part concentrated acid to 1 part water). This solution is now cooled to 0° and a solution (previously cooled to 0°) of 90 g. of technical sodium nitrite in 150 cc. of water is added through a separatory funnel. During the addition of the nitrite solution, mechanical stirring should be employed and the flask cooled well with ice and salt. The addition is made at such a rate (thirty to forty minutes for the entire addition) that the temperature does not rise above 5°. The precipitate of nitroso dimethylaniline hydrochloride is filtered off with suction, then washed with about 300 cc. of diluted hydrochloric acid (1 : 1).

In a 2-l. beaker, 180 g. of technical dimethylaniline, 125 cc. of formaldehyde (technical 40 per cent), and 300 cc. of concentrated hydrochloric acid are mixed and heated for ten

minutes on a steam bath. The mixture is now placed in a hood and the nitroso dimethylaniline added all at once, or as rapidly as possible. The beaker is then covered with a watch glass. A vigorous reaction soon occurs and is complete in about five minutes. The resulting solution is transferred to a 5-l. flask and diluted to 4 l.; stirring is started, and a 25 per cent solution of sodium hydroxide is added until the red color disappears (about 650 cc. are required). The yellow benzylidene compound separates, is filtered with suction and washed with water. The moist precipitate is transferred to a 4-l. glass jar, covered with 1000 cc. of 50 per cent acetic acid and 250 cc. of formaldehyde, and stirred until twenty minutes after the benzylidene compound has gone into solution. While the mixture is being stirred vigorously to prevent lumping of the precipitate, 400 cc. of water and 200 g. of cracked ice are added during the course of five minutes. The dimethylaminobenzaldehyde generally separates gradually in fifteen to twenty minutes, but in some cases does not. If the precipitate does not form, the solution is placed in a refrigerator for a few hours or overnight. The mixture is filtered with suction and washed at least ten times with 300 cc. of water. The precipitate is sucked as dry as possible for fifteen to thirty minutes.

The slightly moist aldehyde is distilled under diminished pressure from an oil bath, by means of a 1-l. Claisen flask. A small amount of water comes over first, then the thermometer rises rapidly to the boiling point of the aldehyde (180°/22 mm.). In changing receivers between the water fraction and the aldehyde, care should be taken to keep the side-arm of the distilling flask warm; otherwise, on starting the distillation again, the aldehyde will solidify in the side-arm and cause trouble. It is advisable not to collect the very last portion of the distillate with the main portion, as the former is frequently quite red. This is best added to crude material from another run. The main distillate is dissolved in 100 cc. of alcohol in a 2-l. beaker, then 1000 cc. of water are gradually added with vigorous mechanical stirring to prevent lumping. The aldehyde separates, and is filtered with suction. The product, when dry, weighs 125–

130 g. (56–59 per cent of the theoretical amount), and melts at 73°.

The aldehyde prepared in this way is in the form of small granular crystals, which vary in different runs from a flesh color to a lemon yellow. For practically all purposes, this slightly colored product is entirely satisfactory and is essentially pure, as can be judged by the melting point. For reagent purposes it is desirable to remove the color completely, particularly since the product obtained as just described has a tendency to take on a reddish tinge on exposure to light. Further purification can be accomplished by dissolving the aldehyde (it dissolves slowly) in dilute hydrochloric acid (1 part of concentrated acid, sp. gr. 1.19, to 6 parts of water), 125 g. of aldehyde requiring 700 cc. of the acid. The solution is placed in a jar and diluted with half its volume of water, and dilute sodium hydroxide solution (15–20 per cent) is added slowly with mechanical stirring. At the beginning, the aldehyde comes down slightly colored. After about 10 to 30 g. are precipitated, however, the product appears white; this point can be readily seen. The first precipitate is filtered off and added to the next run of crude material, or fractionally precipitated again from hydrochloric acid. The rest of the aldehyde is now precipitated by means of more sodium hydroxide solution, and comes down almost white. At the very end of the neutralization, particularly if the original product was quite yellow, the last 4 to 5 g. of aldehyde should be precipitated separately, as they are inclined to be slightly colored. If too much alkali is added towards the end of the neutralization, a brown color appears, but the addition of a little hydrochloric acid will destroy this color. The main portion of the precipitate is filtered and dried; it weighs 95–100 g., m. p. 73°. The succeeding runs yield 115–128 g. of finished product, on account of the extra crude material obtained from the distillation and reprecipitation of the previous run.

## 2. Notes

The aldehyde that is obtained without reprecipitation gradually takes on a pinkish tinge on exposure to light. After the reprecipitation, however, this characteristic disappears.

Thorough washing of the crude aldehyde is particularly desirable, as it removes a reddish impurity which tends to distil over and color the product lemon yellow or sometimes even brownish yellow. When such a brownish product is obtained, it is quite necessary to make a second precipitation, as well as to observe the directions mentioned in the purification of the crude aldehyde, namely, to precipitate the first few grams and the last few grams of the aldehyde separately. The precaution of rejecting the first and last portions of the precipitate is unnecessary in the reprecipitation. In the reprecipitation of a deeply colored product, the portion of aldehyde at the end may be even purplish in color and particular care must be taken to keep this separate.

Vigorous mechanical stirring must be employed during the precipitation of the crude aldehyde, as otherwise large lumps are formed which make washing difficult.

A previous investigator has mentioned that the crude product must be dried before distilling. This, however, is unnecessary. If the aldehyde is dried before distilling, it is possible to use a 500-cc. distilling flask instead of a 1-l. one.

In purifying the aldehyde by dissolving in acid and reprecipitating, it is essential not to use stronger acid than that specified (1 : 6), as stronger acid causes a deepening of the color of the solution. If the concentrated acid, which is to be diluted and used in this procedure, does not have a sp. gr. of 1.19, it will be necessary to add the equivalent amount of weaker acid in order to dissolve the *p*-dimethylaminobenzaldehyde. In purifying the aldehyde, sodium carbonate may be used in place of sodium hydroxide for precipitation, but it causes much foaming.

When the apparatus for distilling, etc., is all set up, a run such as described above requires about five to six hours for completion.

### 3. Other Methods of Preparation

*p*-Dimethylaminobenzaldehyde has been made by the condensation of chloral with dimethylaniline, and subsequent hydrolysis;[1] by the hydrolysis of tetramethyldiaminobenzhydrol with acetic acid;[2] by the condensation of dimethylaniline, formaldehyde and *m*-sulfo-*p*-tolyl hydroxylamine followed by hydrolysis;[3] by the electrolytic reduction of a mixture of sodium nitrobenzene sulfonate, dimethylaniline and formaldehyde, and subsequent hydrolysis;[4] by the reduction of a mixture of dimethylaniline, formaldehyde and sodium nitrobenzene sulfonate with iron and hydrochloric acid, followed by hydrolysis;[5] by the condensation of alloxan with dimethylaniline followed by hydrolysis;[6] by the condensation of dimethylaniline, formaldehyde and sodium *p*-toluidine sulfonate in the presence of hydrochloric acid and potassium dichromate followed by hydrolysis.[7] The most satisfactory method, however, is the condensation of dimethylaniline, formaldehyde and nitroso dimethylaniline, followed by hydrolysis,[8] a method which was first described by E. Noelting and later perfected in detail by L. Baumann.

[1] Ber. **18**, 1519 (1885); **19**, 366 (1886); D. R. P. 61, 551; Frdl. **3**, 109 (1892).
[2] Ber. **27**, 3317 (1894).
[3] D. R. P. 103,578; Frdl. **5**, 101 (1899).
[4] D. R. P. 105,103; Frdl. **5**, 107 (1899).
[5] D. R. P. 105,105; Frdl. **5**, 109 (1899).
[6] D. R. P. 108,026; Frdl. **5**, 117 (1899).
[7] D. R. P. 118,567; Frdl. **6**, 133 (1901).
[8] Ber. **37**, 858 (1904); J. Biol. Chem. **41**, 146 (1920).

## VI

## ETHYL OXALATE

$$(CO_2H)_2 + 2\ C_2H_5OH \rightarrow (CO_2C_2H_5)_2 + 2\ H_2O$$

Prepared by H. T. CLARKE and ANNE W. DAVIS.
Checked by ROGER ADAMS and W. B. BURNETT.

### 1. Procedure

IN a 5-l. flask are placed 1 kg. of crystallized (hydrated) oxalic acid, 1.66 kg. of 95 per cent ethyl alcohol, and 1.33 kg. of

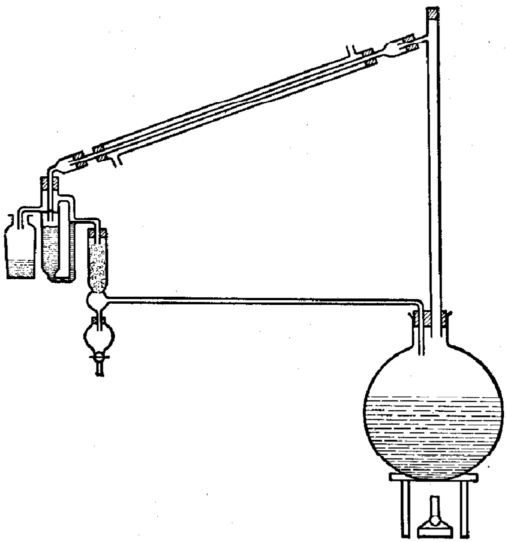


FIG. 1.

carbon tetrachloride. The flask is then fitted with a fractionating column, 1 meter long, to which is attached a condenser and an automatic separator so arranged that the lighter liquid flows

off to a receiver (Fig. 1). The heavier liquid flows through a tower of anhydrous potassium carbonate, and then returns to the reaction flask. The bottom of the tower is connected with a small separatory funnel through which any potassium carbonate solution, which flows from the solid in the tower, may be withdrawn from time to time.

The mixture in the flask is slowly distilled. As soon as about 500 cc. of the lighter liquid has collected, it is placed in a fractionating apparatus and distilled, the material which boils up to 79° being collected separately. This fraction, which consists principally of alcohol, with a little carbon tetrachloride and moisture, is dried with potassium carbonate and returned to the reaction mixture. The higher fractions are redistilled.

The above process is continued until the distillate no longer separates into two phases (about twenty-seven hours). The liquid in the flask is then distilled with the use of a column until the temperature of the vapor reaches 85°; the residue is then distilled under reduced pressure, and the fraction which boils at 106–107°/25 mm. is collected. The yield is 920–960 g. of a colorless liquid (80–84 per cent of the theoretical amount).

## 2. Notes

Water, ethyl alcohol and carbon tetrachloride form a ternary mixture boiling at about 61°. This vapor mixture, on condensation, separates into two phases; the heavier liquid consists of carbon tetrachloride and alcohol with only small amounts of water; the lighter liquid consists of approximately 65 per cent alcohol, 25 per cent water and 10 per cent carbon tetrachloride. By taking advantage of this fact, it is possible to conduct the esterification at a temperature so low that the ethyl hydrogen oxalate first formed does not decompose into ethyl formate and other products, as is the case when the customary methods of esterification are employed.

The reaction may be carried out somewhat more expeditiously if the oxalic acid be dehydrated independently before it is mixed with the alcohol; indeed, it is also possible to remove the bulk

of the water from the alcohol itself by a similar method, before mixing it with the oxalic acid. However, since water is formed during the esterification, little is gained by this procedure.

It is not absolutely necessary to remove the last traces of water from the alcohol-carbon tetrachloride layer by means of potassium carbonate before returning it to the reaction mixture; this process is, however, so simple and requires so little attention that there is no doubt that it is of material aid in cutting down the time of operation. The advantages of using crystallized oxalic acid and commercial 95 per cent alcohol, instead of the anhydrous reagents, are obvious. When technical oxalic acid is used, the yields are usually smaller by 5 to 10 per cent.

The apparatus shown in Fig. 1 may be somewhat more simply constructed by using rubber connections in several places, thus eliminating a certain amount of glass blowing, and making a more flexible piece of apparatus. The side-arm of the separator may be made with two rubber connections,—one above and one below the tube leading to the potassium carbonate tube. The long return tube to the flask may be constructed with a rubber joint very near the carbonate tube and one near the flask.

### 3. Other Methods of Preparation

Ethyl oxalate has been prepared in poor yields by the following methods: by distilling a mixture of anhydrous oxalic acid and absolute alcohol;[1] by heating a mixture of anhydrous oxalic acid and 97 per cent alcohol under a reflux condenser and fractionating the resulting mixture;[2] by distilling a mixture of anhydrous oxalic acid and absolute alcohol, the vapor of absolute alcohol being passed simultaneously into the mixture;[3] by allowing a saturated solution of oxalic acid in alcohol to stand for a long time at 40–50°.[4]

A good yield has been obtained by Anschütz[5] by a method

[1] Jahresb. **1861**, 598.
[2] J. prakt. Chem. (2), **34**, 500 (1886).
[3] Monatsh. **17**, 614 (1896).
[4] Ann. **65**, 350 (1848).
[5] Ber. **16**, 2414 (1883).

involving saturation of a mixture of crystallized oxalic acid and alcohol with hydrogen chloride, removal of the alcohol and water by distillation under reduced pressure, and repetition of the treatment with the alcohol and hydrogen chloride, the process being carried out several times.

# VII

## ETHYL PHENYLACETATE

$$C_6H_5CH_2CN + C_2H_5OH + H_2SO_4 + H_2O \rightarrow C_6H_5CH_2CO_2C_2H_5 + NH_4HSO_4$$

Prepared by ROGER ADAMS and A. F. THAL.
Checked by OLIVER KAMM.

### 1. Procedure

IN a 3-l. round-bottom flask, fitted with an efficient reflux condenser, are mixed 750 g. of 95 per cent alcohol, 750 g. of concentrated sulfuric acid and 450 g. of benzyl cyanide. The mixture, which soon separates into two layers, is heated to boiling over a low flame, for six to seven hours, cooled and poured into 2 l. of water, and the upper layer is separated. This is washed with a little 10 per cent sodium carbonate solution to remove small amounts of phenylacetic acid which may have been formed, and then distilled *in vacuo*. A small amount of water goes over first and then a pure product boiling 132–138°/32 mm. (120–125°/17–18 mm.). The yield varies in general between 525 and 550 g. (83–87 per cent of the theoretical amount).

### 2. Notes

The benzyl cyanide can be most conveniently prepared according to the directions in preparation III (p. 9); the product which boils over a 5° range should be used.

In washing the layer of ethyl phenylacetate with sodium carbonate it is sometimes advisable to add a certain amount of sodium chloride so that the ester will separate more readily.

The product obtained is water-clear and practically colorless. Although the product is collected over a 5° range, most of the

liquid is found to boil over a 1° range, if distilled slowly without superheating.

The boiling point of ethyl phenylacetate is near that of benzyl cyanide. However, a Kjeldahl analysis of the product shows that only a trace of nitrogen compounds is present.

### 3. Other Methods of Preparation

Ethyl phenylacetate may be prepared by the treatment of benzyl cyanide with alcohol and hydrochloric acid gas.[1] It is much more convenient in the laboratory, however, to use sulfuric acid in place of hydrochloric acid; in fact, the yields obtained are better than those recorded in the literature. This ester may also be made by the esterification of phenylacetic acid with hydrochloric acid and alcohol;[2] or with alcohol and sulfuric acid;[3] the following less important methods of preparation may be mentioned; the action of benzyl magnesium chloride upon ethyl chlorocarbonate,[4] and the action of copper on a mixture of bromobenzene and ethyl chloroacetate at 180°.[5]

[1] Ber. **20**, 592 (1887); Ann. **296**, 361 (1897).
[2] Ber. **2**, 208 (1869).
[3] Ann. **296**, 2, footnote (1897); Compt. rend. **152**, 1855 (1911).
[4] Ber. **36**, 3088 (1903).
[5] Ber. **2**, 738 (1869).

VIII

# GLYCEROL $\alpha, \gamma$-DICHLOROHYDRIN

$$C_3H_5(OH)_3 + 2\,HCl \rightarrow CH_2ClCHOHCH_2Cl + 2H_2O$$

Prepared by J. B. Conant and O. R. Quayle.
Checked by O. Kamm and A. O. Matthews.

## 1. Procedure

One kilo of 90 per cent glycerol (sp. gr. 1.243) and 20 g. of acetic acid are placed in a weighed 2-l. flask which is immersed in an oil bath heated to 100–110°. The flask is fitted with a two-hole stopper, which carries a long tube reaching to the bottom of the flask and a short exit tube. The former is connected to a hydrogen chloride generator, the latter to a catch-bottle and some system for absorbing any excess of hydrogen chloride. A stream of dry hydrogen chloride is passed into the mixture. The absorption of gas is very rapid at the start, but gradually falls off towards the end of the reaction; the stream of hydrogen chloride should be regulated accordingly. The flask is removed from time to time and weighed; when the absorption of gas practically ceases, the increase in weight will be about 875 g. (25 per cent more than the theoretical amount).

The product is now cooled, placed in a 4-l. beaker, and treated with solid sodium carbonate until just alkaline to litmus. Water is added from time to time, to facilitate the reaction with the sodium carbonate and to prevent the separation of salt; about 500 cc. are required. The mixture is transferred to a separatory funnel and the aqueous layer separated. The crude dichlorohydrin, which weighs 1250 g., is distilled *in vacuo*. The first fraction boiling below 68°/14 mm. weighs 225 g., and consists of water and some dichlorohydrin; the dichlorohydrin is collected between 68–75°/14 mm., and weighs about 775 g. The water

is separated from the first fraction, which is then redistilled and yields 100 g. of dichlorohydrin. A still further amount of material (40–45 g.) may be obtained by extracting with benzene, the aqueous layer obtained in the neutralization process. This is, however, hardly profitable. The neutralization and distillation will require about four hours.

The 875 g. of dichlorohydrin thus obtained boils over a 7° range; this is 70 per cent of the theoretical amount. Redistillation yields 700–720 g. boiling 70–73°/14 mm. (57 per cent of the theoretical amount).

## 2. Notes

The most convenient hydrogen chloride generator is that described by Sweeney.[1] Concentrated hydrochloric acid is introduced into concentrated sulfuric acid, by means of a dropping funnel and a *capillary tube leading to the bottom of the sulfuric acid container.* It is convenient to use a 3-l. bottle for this container and a 1-l. funnel to contain the hydrochloric acid. The gas is dried by passing through a wash-bottle containing concentrated sulfuric acid. An empty catch-flask should be connected between the generator and the absorption flask in case any glycerol tends to suck back at the start of the reaction. About 6 kg. of concentrated hydrochloric acid and 10 kg. of concentrated sulfuric acid are required in one run. The generating flask will have to be recharged every six hours; it should be half filled with sulfuric acid. Aside from this, the apparatus needs no attention. The oil bath can be conveniently heated on an electric hot plate.

The dichlorohydrin boiling over a 7° range is sufficiently pure for most purposes. It contains very little, if any, isomeric dichlorohydrin, since on oxidation it gives dichloroacetone in good yields.

## 3. Other Methods of Preparation

The following methods of preparing dichlorohydrin are described in the literature: the action of gaseous hydrogen

[1] J. Am. Chem. Soc. **39**, 2187 (1917).

chloride on glycerol;[1] the action of gaseous hydrogen chloride on glycerol mixed with an equal volume of acetic acid;[2] the action of hydrogen chloride gas on glycerol containing 1–2 per cent of some organic acid, as acetic, as a catalyst;[3] the action of aqueous solution of hydrochloric acid on glycerol containing acetic acid as a catalyst;[4] the action of sulfur monochloride on glycerol.[5]

The previous work, described in the literature, indicated that the best yields were obtained by the treatment of glycerol containing 1–2 per cent of acetic acid as a catalyst by gaseous hydrogen chloride. Therefore this method was employed.

[1] Ann. **88**, 311 (1853); Ann. chim. phys. (3) **41**, 297 (1854); (6), **22**, 437 (1891); Bull. soc. chim. (2), 48, 237 (1887); Z. physik. Chem. **92**, 717 (1918); **93**, 59 (1919); **94**, 691 (1920); D. R. P. 263,106; 272,337; Frdl. **11**, 33 (1912).

[2] Ann. Spl. **1**, 218 (1861); Ann. chim. phys. (3) **60**, 18 (1860).

[3] D. R. P. 197,308; Frdl. **9**, 33 (1908).

[4] D. R. P. 197,309; Frdl. **9**, 33 (1908).

[5] Ann. **122**, 73 (1862); **168**, 43 (1873); Ber. **5**, 354 (1872); Ann. chim. phys. (6) **22**, 437 (1891).

# IX

## GLYCEROL $\alpha$-MONOCHLOROHYDRIN

$$C_3H_5(OH)_3 + HCl \rightarrow CH_2ClCHOHCH_2OH + H_2O$$

Prepared by J. B. CONANT and O. R. QUAYLE.
Checked by O. KAMM and A. O. MATTHEWS.

### 1. Procedure

FIVE HUNDRED grams of glycerol (90 per cent) and 10 g. of glacial acetic acid are mixed in a weighed 1-l. flask, which is placed in an oil bath heated to 105–110°. A rapid stream of dry hydrogen chloride is introduced into the mixture. The flask is removed from the bath from time to time and reweighed. At the end of about four hours the flask will have gained 190 g. in weight. The reaction is then complete.

The product is distilled under diminished pressure. Below 114°/14 mm., 220–250 g. distil; this portion is mostly water. The monochlorohydrin is collected between 114–120°/14 mm.; it weighs 360 g., which is 66 per cent of the theoretical amount. About 20 g. more may be obtained by neutralizing the first fraction and separating the aqueous layer.

### 2. Notes

The same apparatus is employed as in the preparation of dichlorohydrin (preparation VIII, p. 29).

The portion boiling 120–130°/14 mm. only amounts to 15–30 g., showing that very little of the $\beta$-compound is formed. This is further shown by the fact that the dichlorohydrin formed by continued action of hydrogen chloride under the same conditions contains very little, if any, $\alpha$, $\beta$ dichloride.

Two kilograms of concentrated sulfuric acid and 750 g. of concentrated hydrochloric acid are sufficient to produce the necessary amount of hydrogen chloride.

A light straw-colored final product is obtained in some cases.

An alternative procedure which is slower and gives slightly lower yields, but does not require a hydrogen chloride generator, is as follows:

Three hundred grams of glycerol, 600 cc. of hydrochloric acid (sp. gr. 1.19) and 15 g. of glacial acetic acid are heated under a reflux condenser for ten hours, in a 2-l. flask. The boiling should be very gentle in the early stage of the reaction, as considerable hydrochloric acid vapor is evolved. As the reaction progresses, and the evolution of acid vapors diminishes, the mixture is more strongly heated.

The reaction products are distilled under ordinary pressure until the temperature of the liquid has reached 140° (thermometer bulb immersed in the liquid). The residual products are distilled under diminished pressure, and the following fractions obtained. (1) Up to 115°/11 mm.; (2) 115–117°/11 mm.; (3) 117–170°/11 mm. (1) is mostly aqueous hydrochloric acid; (2) is the monochlorohydrin; and (3) is glycerol. The second portion is redistilled and the portion boiling at 115–118°/11 mm. or 133–136°/20 mm. is collected. The yield is 190–205 g., 53–57 per cent of the theoretical amount.

### 3. Other Methods of Preparation

The following methods of preparing monochlorohydrin are described in the literature: action on glycerol of gaseous hydrogen chloride;[1] action of gaseous hydrogen chloride on glycerol mixed with an equal volume of acetic acid;[2] action of aqueous hydrochloric acid on glycerol[3] alone or with an organic acid (1–2 per cent), such as acetic, as a catalyst;[4] gaseous hydrogen

[1] Ann. **88**, 311 (1853); Ann. chim. phys. (3) **41**, 207 (1854); D. R. P. 254,709; 269,657; Frdl. **11**, 31 (1912).

[2] Ann. chim. phys. (3) **60**, 18 (1860).

[3] D. R. P. 180,668; Frdl. **8**, 27 (1907); J. Am. Chem. Soc. **42**, 2096 (1920).

[4] D. R. P. 197,309; Frdl. **9**, 34 (1908).

chloride with an organic acid, as acetic, as a catalyst;[1] gaseous hydrogen chloride with the ester of an organic or inorganic acid as a catalyst;[2] the action of sulfur monochloride on glycerol.[3]

[1] D. R. P. 197,308; Frdl. **9**, 33 (1908).
[2] D. R. P. Anm. 23,510; 16,579; Frdl. **9**, 36 (1908).
[3] D. R. P. 201,230; Frdl. **9**, 35 (1908).

# X

## HYDRAZINE SULFATE

$$2\,NH_3 + NaOCl \rightarrow NH_2NH_2 + H_2O + NaCl$$

Prepared by Roger Adams and B. K. Brown.
Checked by J. B. Conant and W. L. Hanaway.

### 1. Procedure

A normal solution of sodium hypochlorite is prepared as follows: in a 5-l. round-bottom flask are placed 1800 g. of sodium hydroxide solution (300 g. of sodium hydroxide to 1500 g. of water) and 1500 g. of ice. Chlorine gas is then passed into the solution until it has gained in weight approximately 213 g. During this addition, the solution must be kept thoroughly cooled with ice, in order that chlorates will not be formed. After all the chlorine has been passed in, it is necessary to be certain that the mixture is slightly alkaline, since any excess of free chlorine in the solution prevents the formation of hydrazine.

In a 14-inch evaporating dish are placed 1500 cc. of c. p. ammonia water (sp. gr. 0.90), 900 cc. of distilled water, 375 cc. of 10 per cent gelatine solution, and 1200 cc. of the normal sodium hypochlorite solution prepared as above. This mixture is heated as rapidly as possible and boiled down until one-third of the original volume is left. This solution is then cooled thoroughly with ice and filtered with suction, first through two layers of toweling and then through one thickness of ordinary filter paper over cloth, in order to remove finely divided solid impurities. The solution is then placed in a precipitating jar, and cooled down thoroughly (0°) with ice and salt; 10 cc. of concentrated sulfuric acid for each 100 cc. of solution are gradually added with constant stirring. A precipitate of

hydrazine sulfate ($NH_2NH_2 \cdot H_2SO_4$) forms. The mixture is allowed to stand in the cold for a few hours in order to complete the precipitation, and is then filtered by suction in the usual way and washed with cold alcohol. The yield varies from 53 g. to 58 g. per 1500 cc. of ammonia water (34–37 per cent of the theoretical amount). The product is perfectly white and crystalline, and satisfactory for almost any purpose. If an absolutely pure product is desired, it must be recrystallized from water. For every 21 g. of crude product, 100 g. of boiling water are used. If the crude hydrazine is brown, it is advisable to use a little bone-black. After the mixture has been filtered and cooled to 0°, 19 g. of pure white crystals are obtained.

### 2. Notes

In the preparation of the sodium hypochlorite solution it is quite necessary that the mixture be kept cold and be alkaline to red litmus paper at the end of the reaction, if good yields of hydrazine are to be obtained.

Since iron is an anti-catalyzer, it is necesssary to use distilled water throughout the process.

As a viscolizer, a substance such as starch, glycerol, glue or gelatine may be used; the last, however, gives by far the most satisfactory results.

In order to obtain a pure white hydrazine sulfate as the first precipitate, it is necessary to cool the hydrazine solution thoroughly and filter it twice before the sulfuric acid is added. Moreover, the sulfuric acid must be added slowly and with stirring. If these conditions are not followed, material containing brown particles results.

The mother liquor obtained from the crystallized hydrazine sulfate contains a small amount of hydrazine. If 200 g. of copper sulfate are dissolved in water and added to 10 l. of the filtrates from the above processes, a light-blue crystalline precipitate of the double salt of copper sulfate and hydrazine sulfate will be formed after ten hours. This salt, when suspended in ten times its weight of distilled water and treated with hydrogen sulfide,

decomposes into copper sulfide and hydrazine sulfate. After the copper salt has been filtered off, the solution is concentrated until the hydrazine sulfate crystallizes. The yield of product is small, so that it is hardly advisable to undertake this recovery in the laboratory.

It is possible for one man, simultaneously evaporating six dishes of the hydrazine mixture, to turn out from 20 to 25 runs in nine hours. The time for the evaporation of a solution, such as is mentioned in the experimental part, with a four-flame Bunsen burner, is two to three hours; if the evaporation is carried out more slowly than this, the yield of product is distinctly diminished.

### 3. Other Methods of Preparation

Hydrazine salts have been prepared by the action of hypochlorites on ammonia[1] or urea;[2] by the hydrolysis of salts of sulfohydrazimethylene disulfonic acid;[3] by the hydrolysis of triazoacetic acid;[4] by the reduction of diazoacetic ester;[5] by the reduction of nitroguanidine followed by hydrolysis;[6] by the reduction of the nitroso derivatives of hexamethylene tetramine;[7] by the reduction of nitrates or nitrites with zinc in neutral solution;[8] by the action of sodium bisulfite on hyponitrous acid

[1] D. R. P. 192,783; Chem. Zentr. **1908** (I), 427; Chem. Ztg. **31**, 926 (1907); D. R. P. 198,307; Chem. Zentr. **1908** (I), 1957; Eng. Pat. 22,957; C. A. **2**, 1999 (1908); U. S. Pat. 910,858; C. A. **3**, 1065 (1909); French Pat. 382,357; C. A. **3**, 2358 (1909); Ber. **40**, 4588 (1907); Laboratory Manual of Inorganic Preparations, by A. B. Lamb, Harvard University, Cambridge, Mass.

[2] J. Russ. Phys. Chem. Soc. **37**, 1 (1905); Chem. Zentr. **1905** (I) 1227; D. R. P. 164,755; Frdl. **8**, 53 (1905); French Pat. 329,430; J. Soc. Chem. Ind. **22**, 1063 (1903); Chem. Zentr. **1905** (I) 1227.

[3] D. R. P. 79,885; Frdl. **4**, 26 (1895); Ber. **28**, 2381 (1895).

[4] Ber. **20**, 1632 (1887); Chem. News **55**, 288 (1887); D. R. P. 47,600; Frdl. **2**, 554 (1889); J. prakt. Chem. (2) **39**, 27 (1889).

[5] Ber. **27**, 775 (1894); **28**, 1848 (1895); D. R. P. 58,751; Frdl. **3**, 15 (1891); D. R. P. 87,131; Frdl. **4**, 28 (1896).

[6] Ann. **270**, 31 (1892); D. R. P. 59,241; Frdl. **3**, 16 (1891); Eng. Pat. 6,786; J. Soc. Chem. Ind. **11**, 370 (1892).

[7] D. R. P. 80,466; Frdl. **4**, 27 (1895); Ann. **288**, 232 (1895).

[8] Eng. Pat. 11,216; J. Soc. Chem. Ind. **14**, 595 (1895).

followed by reduction;[1] by the reduction of $K_2SO_3N_2O_2$;[2] by the action of ammonia on dichlorourea;[3] by the reduction of nitrosoparaldimin;[4] by the action of copper sulfate on ammonia at high temperatures;[5] by the reduction of methylene diisonitrosoamine;[6] by the hydrolysis of the addition product of diazoacetic ester and fumaric or cinnamic esters.[7]

[1] Ber. **33**, 2115 (1900); Ann. **288**, 301 (1895).

[2] Ber. **27**, 3498 (1894).

[3] J. Chem. Soc. **95**, 235 (1909); Chem. News **98**, 166 (1908).

[4] Ber. **23**, 752 (1890).

[5] Chem. News **66**, 223 (1892).

[6] Ber. **27**, 3292 (1894);

[7] Ber. **21**, 2637 (1888).

# XI

## MESITYLENE

$$3\ CH_3COCH_3 + (H_2SO_4) \rightarrow C_6H_3(CH_3)_3 + 3\ H_2O$$

Prepared by Roger Adams and R. W. Hufferd.
Checked by H. T. Clarke and W. W. Hartman.

### 1. Procedure

In a 12-l. round-bottom flask, arranged so that the contents can be mechanically stirred, are placed 4600 g. (5750 cc.) of technical acetone. The flask is then well cooled with an ice-and-salt mixture, until the temperature of the acetone is between 0° and 5°. Stirring is started, and 4160 cc. of commercial concentrated sulfuric acid is run in at such a rate that the temperature of the mixture never rises above about 10°. This addition is accomplished in about five to ten hours. The stirring is continued for three to four hours longer, while the flask still remains immersed in the original freezing mixture to which no further amount of ice is added. The mixture is then allowed to stand at room temperature for eighteen to twenty-four hours.

A 5-l. round-bottom flask is fitted with a rubber stopper or a cork stopper coated with pitch, carrying two glass tubes, one of which (for the entrance of steam) reaches to the bottom of the flask, while the other extends into the open end of a condenser set for downward distillation. The stopper should be wired into the flask. The glass delivery tube into the condenser should not be less than a 12-mm. bore, and the condenser should consist of two 120-cm. water-cooled condensers attached end to end. To the end of the condensing system, an adapter is attached, the small end of which is at least 8 mm. in bore and is fitted tightly into a stopper in a 2-l. suction flask. To the side-

arm of the suction flask is attached a tube leading to an exhaust fan, in order to carry away the gases which are evolved during the subsequent distillation. In the 5-l. flask are placed about 2 l. of the sulfuric acid-acetone reaction mixture, and the flask is then heated with a free flame and shaken occasionally. A reaction starts at the end of about fifteen or twenty minutes, as shown by the evolution of gas (chiefly sulfur dioxide), and is allowed to run for about three minutes. At the end of this time, a current of steam is passed in and continued for about three minutes. During this period a large proportion of the mesitylene distils and should be kept separate from the subsequent distillate. The steam distillation is continued at such a rate that about 800 cc. distils in twenty-five to thirty minutes and is collected as a second distillate. At the end of this time, the distillation is stopped, the water poured off from the distilling flask and the tarry material emptied out while hot into waste jars. The total amount of original reaction mixture requires five distillations similar to the one just described. The first distillates from each of the five distillations are mixed, and the layer of mesitylene is separated from the water. This is shaken with sodium hydroxide solution until no more odor of sulfur dioxide is noticeable, then washed twice with water and distilled. The first portion of the distillate consists of a small amount of water and mesitylene and is added to the combined second distillates. The fraction which distils up to 210° is saved. The second distillates are combined, washed in the same way as the first and then distilled; the fraction which distils up to 210° is combined with the corresponding fraction from the first distillates.

These combined fractions (which boil up to 210°) and 15 g. of sodium are placed in a 2-l. distilling flask, the side-arm of which is closed with a rubber tube and pinchcock and which is fitted with a reflux condenser. The mixture is heated just below the boiling point for about three hours, during which time the impurities are attacked by the molten sodium, and a gelatinous, reddish mass forms. The reflux condenser is now removed and one set for downward distillation is attached to the side-arm. The mixture is distilled and about two-thirds of the liquid

removed in this way. The residue is cooled, the liquid poured off from solid material and distilled up to 210°.

The distillates from the sodium treatment are now fractionated with a good column (at least 30 cm. long), and the portion which boils at 163–167° is collected. The yield of this fraction varies in different runs from 430 to 470 g. (13–15 per cent of the theoretical amount), but very often will be as high as 500 g., and has reached, in certain experiments, 600 g.

An alternative method for the purification of the crude material has been employed by Clarke and Hartman, and yields a slightly higher-grade product than the sodium method. It is as follows:

The combined distillates are treated with an equal volume of concentrated sulfuric acid and the solution warmed on a water bath for an hour, under a reflux condenser, with occasional shaking or, better, with mechanical stirring. Upon cooling, mesitylene sulfonic acid crystallizes and the unsulfonated material remains as an oil on the surface. The mixture is filtered through flannel or a "filtrose" plate, and the crystals are washed with 60–70 per cent sulfuric acid. The oily layer is again warmed with sulfuric acid, as before. The acid and oily filtrates from the two sulfuric acid treatments are steam distilled, and the distillate combined with the next batch of material. The crystals are mixed with 2 l. of 15 per cent hydrochloric acid and heated under a reflux condenser for two to three hours. The reaction mixture is now steam distilled, the mesitylene separated, dried over calcium chloride and fractionated; the portion which boils at 163–167° is collected.

## 2. Notes

The cooling of the reaction flask must be very efficient, a 10–15 cm. blanket of a thorough mixture of ice and salt being used. If this precaution is not employed, the time for the addition of the sulfuric acid is greatly increased, provided the temperature of the reaction mixture is still kept within the limits mentioned.

If a cork is used for the steam distillation of the reaction

mixture of acetone and sulfuric acid, it should be coated well with pitch and wired into the flask. This is necessary because the vapors of the reaction mixture attack an ordinary cork very badly, and soften it so much that it is necessary to rewire it to prevent it from slipping out. A rubber stopper is satisfactory and may be used in several runs.

The evolution of gas is so vigorous that it is not possible to distil more than 2 l. of the original reaction mixture at one time in the apparatus described. The connections on the apparatus, in which the mesitylene is obtained from the crude reaction mixture, should be tight, since the fumes evolved during the heating are very irritating.

The product which distils during the initial heating and the three minutes of steam distillation is mainly satisfactory material; the rest of the steam distillation yields only a small amount of pure product. The two portions of the distillate are, therefore, kept separate, since the second distillate always contains a considerable amount of high-boiling product which tends to cause emulsification of the alkali in the purification. No recovery of acetone is made.

The mechanism of the reaction is undoubtedly as follows: when the sulfuric acid and acetone are in contact for long periods of time, several molecules of the acetone condense to form aldol condensation products. These do not break down into mesitylene until the temperature is raised in the second part of the experiment.

While the original reaction mixture is standing, the temperature gradually rises to 40° or 50° in the course of six to ten hours, and then gradually cools off again. It is probable that at the end of this time (when the flask has cooled again) the reaction mixture could be distilled with nearly as good a yield as is obtained after standing eighteen to twenty-four hours.

The wide variation in yields which are mentioned in the experimental part is probably due to a slight change in the grade of the chemicals which are used in this preparation.

### 3. Other Methods of Preparation

The cheapest and most convenient method by which mesitylene may be prepared is by the action of a dehydrating agent upon acetone; the agent most commonly used is sulfuric acid.[1] It has been shown also that phosphoric acid will convert acetone to mesitylene.[2] A number of other methods have also been used for the preparation of mesitylene: the action of sulfuric acid on methyl acetylene;[3] the action of sulfuric acid on mesityl oxide and phorone;[4] the action of aluminium chloride on methyl chloride and benzene;[5] the action of mineral acids upon mesitoyl or benzoyl mesitylene;[6] the action of phosphoric acid upon diaceto-mesitylene;[7] the treatment of methylene-3-dimethyl-1, 5-cyclo-hexene-1 with bromine and then with alcoholic potash.[8]

[1] Ann. **141**, 131 (1867); **147**, 43 (1868); **278**, 210 (1893); Bull. soc. chim. (2) **40**, 267 (1883); J. prakt. Chem. (1) **15**, 129 (1838); Am. Chem. J. **15**, 256 (1893); **20**, 807 (1898).

[2] J. Chem. Soc. **99**, 1251 (1911).

[3] Ber. **8**, 17 (1875).

[4] Ber. **7**, 1169 (1874); **10**, 858 (1877).

[5] Ber. **12**, 329 (1879); Ann. chim. phys. (6) **1**, 461 (1884).

[6] Ber. **32**, 1910 (1899).

[7] Ber. **32**, 1563 (1899).

[8] Ber. **43**, 3093 (1910).

# METHYL RED

$$(o)HO_2CC_6H_4NH_2+HNO_2+HCl \rightarrow (o)HO_2CC_6H_4N_2Cl+H_2O$$

$$(o)HO_2CC_6H_4N_2Cl+C_6H_5N(CH_3)_2 \rightarrow (o)HO_2CC_6H_4N{=}NC_6H_4N(CH_3)_2+HCl$$

Prepared by H. T. CLARKE and W. R. KIRNER.
Checked by ROGER ADAMS and J. B. DAVIS.

## 1. Procedure

TECHNICAL anthranilic acid (generally about 95 per cent pure) (685 g.) is dissolved in 1.5 l. of water and 500 cc. of concentrated hydrochloric acid (sp. gr. 1.17), by heating. The insoluble dark impurity present in small amounts is filtered off, and the filtrate is transferred to a 16-l. crock and chilled with stirring. It is then mixed with a mush of 2.5 kg. of ice and 750 cc. of concentrated hydrochloric acid. The crock is cooled externally with ice, and the contents stirred continuously. When the temperature reaches about 3°, a filtered solution of 360 g. of sodium nitrite in 700 cc. of water is dropped in slowly, through a long capillary tube reaching below the surface of the liquid, until a faint but permanent reaction to starch potassium iodide paper is obtained; the temperature is kept between 3° and 5°. This operation requires all but about 30 cc. of the nitrite solution and occupies one and a half to two hours. To the solution of the diazonium salt are now added 848 g. of dimethylaniline; this may be done rapidly, as the temperature does not rise appreciably. Stirring is continued for one hour, the temperature being kept at 5°. Five hundred cc. of a filtered solution of

680 g. of crystallized sodium acetate diluted to 1200 cc. are then added, and the stirring continued for four hours. If a foamy solid rises to the surface during this time and refuses to become incorporated by the stirrer, a few drops of ethyl acetate may be added to reduce the foam. The mixture is allowed to stand overnight in an ice bath which is well insulated by several thicknesses of burlap; the temperature must be kept below 7° to get a good yield of product. The remainder of the sodium acetate solution is then added with stirring, and after the mixture has been stirred for an additional period of one to three hours, the temperature is allowed to rise slowly to 20–25° in the course of twenty-four hours. Just enough sodium hydroxide solution is then added, with stirring, to cause the mixture to have a distinct odor of dimethylaniline (about 240 cc. of a 40 per cent solution are generally required), and the mixture is allowed to stand for forty-eight hours or longer at room temperature (20–25°).

The solid is then filtered off, washed first with water, then with 400 cc. of 10 per cent acetic acid (to remove the dimethylaniline) and finally with distilled water. The last filtrate is generally pale pink. The solid is sucked as dry as possible, spread out on a tray in order to allow most of the water to evaporate (fifteen to twenty hours) and then suspended in 4 l. of methyl alcohol in a 12-l. flask. This mixture is stirred on the steam bath under a reflux condenser for one to two hours, allowed to cool slowly, and then chilled in an ice bath and filtered. The solid product is washed with a second 4 l. of cold methyl alcohol. After being dried in air, the product varies in weight from 820 to 870 g.

The product is extracted with boiling toluene in the following manner: 150 g. are placed in a fluted filter paper of 29 cm. diameter in a 25-cm. glass funnel which passes through the cork of a 2-l. flat-bottom conical flask containing 1250 cc. of toluene (Fig. 2). The flask is heated on an electric stove, and a 12-l. round-bottom flask is placed on the funnel to act as a condenser, cold water being run through the flask. The toluene is boiled until the condensed liquid runs through almost colorless (this requires from four to ten hours). The heating is then discontinued,

and, as soon as the liquid ceases to boil, the flask is removed to a bath containing water at 90–100°; the level of the water should be slightly above the level of the liquid in the flask. This arrangement permits the temperature to fall slowly so that large crystals are obtained. In the meantime a second conical flask containing 1250 cc. of toluene is attached to the funnel, and a new charge of 150 g. of crude methyl red is placed in the paper. When extraction is complete it is found that a certain amount of black

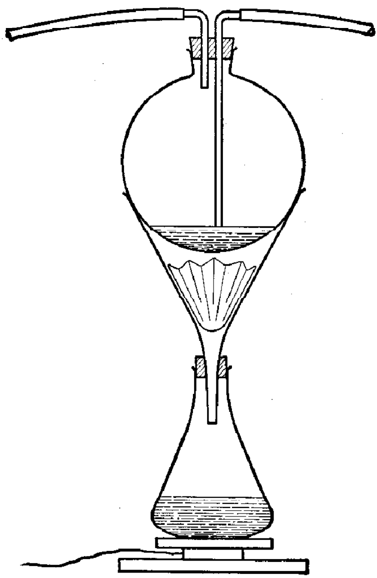


FIG. 2.

amorphous insoluble matter remains on the filter; this is discarded. The crystals of methyl red are filtered off and washed with a little toluene. The weight of pure material is 755–805 g. The mother liquors are concentrated to one-fourth of their volume, and the crystals which separate on cooling are recrystallized from fresh toluene. The recovered toluene can, of course, be employed again. The total yield of pure methyl red is 790–840 g. It melts at 181–182°.

The watery mother liquors from the crude methyl red are

rendered alkaline with sodium hydroxide and distilled until no more dimethylaniline passes over. In this way 250 to 400 g. of moist dimethylaniline are recovered.

## 2. Notes

The amount of hydrochloric acid indicated must not be reduced; otherwise, diazoamino compounds are formed.

It is essential to keep the temperature low while unreacted diazobenzoic acid remains in solution, in order to avoid decomposition. If this precaution is not taken, the yields are considerably diminished, through the formation of tarry by-products.

The use of a capillary tube for the addition of sodium nitrite prevents loss of nitrous acid by local reaction at the surface of the acid solution. The tube should not be tightly connected to the dropping funnel, but should be so arranged that air is sucked through with every drop. In this way, the entrance of the acid liquor into the capillary is prevented.

The formation of the azo compound takes place slowly on the addition of the dimethylaniline, but the speed of the reaction is greatly increased when the hydrogen ion concentration is lowered by the addition of the sodium acetate. It is nevertheless necessary to allow the reaction mixture to stand a long time; if the product be filtered off after only twenty-four hours, a further quantity of dye will separate from the filtrate on standing. The hydrochloride of methyl red is only sparingly soluble in cold water, and is apt to separate in blue needles if the acidity is not sufficiently reduced.

The alcoholic filtrate, obtained on digesting and washing the crude methyl red, contains a more soluble red by-product which gives a brownish-yellow solution in alkali. The methyl alcohol may be recovered with very little loss by distillation; it is, however, impracticable to attempt to recover any methyl red from the residue, owing to the tarry nature of the by-product. The proportion of this by-product is greatly increased if the temperature of the mixture is allowed to rise too soon after the addition of the sodium acetate.

Methyl red is described as crystallizing in needles from glacial acetic acid; on recrystallization from toluene it separates in plates.

When the methyl red is crystallized from toluene, it sometimes separates in the form of bright-red lumps, probably on account of too rapid crystallization. Under these conditions it is advisable to crystallize again, using a somewhat larger amount of toluene.

It is advisable to titrate the crude anthranilic acid with standard alkali and phenolphthalein before starting the experiment. In checking these directions, an 80 per cent anthranilic acid was used; it gave a correspondingly lower yield of methyl red (650–700 g.). The yield of methyl red is about 65 to 70 per cent based on the dimethylaniline actually used up, but only 58–63 per cent based on the anthranilic acid actually present in the technical anthranilic acid employed.

## 3. Other Methods of Preparation

Methyl red was first prepared [1] by diazotization of anthranilic acid in alcoholic solution, the product being allowed to react with dimethylaniline in the same solvent. It has been stated [2] that this process does not work satisfactorily and yields a different product, of brownish-red color.

The preparation of methyl red in aqueous solution has been described by two workers, one of whom [3] gives but few details and claims a nearly quantitative yield; the other [4] gives fuller details and states the yield to be 43.1 per cent of the theory. The recrystallization of methyl red from toluene is stated [5] to yield a product melting at 183°.

[1] Ber. **41**, 3905 (1908).
[2] Chem. Zentr. **1910**, (I), 960; **1910**, (II), 1561.
[3] J. Chem. Soc. **97**, 2485 (1910).
[4] C. A. **14**, 3406 (1920).
[5] J. Chem. Soc. **99**, 1334 (1911).

# XIII

## *p*-NITROBENZOIC ACID

$$(p)NO_2C_6H_4CH_3 + 3O(Na_2Cr_2O_7 + H_2SO_4) \rightarrow (p)NO_2C_6H_4CO_2H + 3H_2O$$

Prepared by O. KAMM and A. O. MATTHEWS.
Checked by H. T. CLARKE and W. W. HARTMAN.

### 1. Procedure

IN a 5-l. round-bottom flask, fitted with a mechanical stirrer, are placed 680 g. of sodium dichromate, 1500 cc. of water, and 230 g. of *p*-nitrotoluene. Stirring is started, and 1700 g. of concentrated sulfuric acid are allowed to flow in during about thirty minutes. The heat of dilution of the sulfuric acid will cause the nitrotoluene to melt, and rapid oxidation will soon take place. The last half of the sulfuric acid must be added gradually, in order to prevent too violent a reaction. Since a small amount of nitrotoluene is volatilized, it is advisable to carry on this work under a hood.

After the sulfuric acid has been added and the spontaneous heating of the reaction mixture has subsided, the mixture is heated to gentle boiling for about half an hour. After the reaction mixture has cooled, 2 l. of water are added, the cooled solution is filtered through a cloth filter, and the product washed with about 1 l. of water. In order to remove the chromium salts as completely as possible, the crude nitrobenzoic acid is warmed on the water bath and agitated with 1 l. of dilute (5 per cent) sulfuric acid solution. After cooling, the product is again filtered. It is then dissolved in 5 per cent sodium hydroxide solution, filtered from any chromium hydroxide remaining, and also from unchanged nitrotoluene. The filtrate, which should be light yellow or greenish in color, is acidified with dilute sulfuric acid, with stirring. It is usually preferable to run the

alkaline solution into the dilute sulfuric acid, rather than to use the reverse procedure, for the precipitation of the nitro acid. The precipitated product is filtered with suction, washed thoroughly, and dried. The product should possess only a light-lemon color. The yield should be 230–240 g. (80–85 per cent of the theoretical amount).

For a product of special purity, crystallization from benzene is advisable. For most purposes, however, the nitrobenzoic acid may be used without crystallization, since its melting point is found to be within 2° of the correct value of 238°.

## 2. Notes

The above procedure differs from that recorded in the literature, mainly in the use of a fairly large excess of sulfuric acid. This shortens the reaction time from forty hours to about one hour, which is especially convenient in the preparation of the acid on a laboratory scale. Because of the use of this large excess of sulfuric acid, the reaction is apt to be rather violent if the directions given are not carefully followed. The oxidation should be carried out under a hood. Small amounts of nitrotoluene are lost by volatilization, but this loss is not serious, as can be seen from the yield of product obtained.

Ten or 20 g. of unchanged nitrotoluene can be recovered from the reaction mixture by steam distillation, but the value of the by-product would not pay for the time spent in recovery.

The washing of the crude reaction product with dilute sulfuric acid is advisable, if good material is to be obtained. If an efficient centrifuge is available for use at this stage of the operation, this separate washing may prove to be less essential.

When a sparingly soluble organic acid is precipitated from fairly concentrated solution, the precipitate is liable to carry down with it some of the salt of the organic acid. Addition of the salt solution to the mineral acid, with stirring, avoids this difficulty.

### 3. Other Methods of Preparation

The nitration of benzoic acid produces only very small yields of the *p*-nitro product.[1] The only practical method for the preparation consists in the oxidation of *p*-nitrotoluene, although for this purpose various oxidizing agents are used. In addition to nitrotoluene, *p*-nitrobenzyl alcohol, *p*-nitrocinnamic acid and similar compounds may be oxidized, but their cost is prohibitive in comparison with that of the cheaper nitro hydrocarbon.

*p*-Nitrotoluene may be oxidized by means of strong nitric acid,[2] chromic acid mixture,[3] or permanganates.[4] Electrolytic oxidation[5] has also been proposed. The procedure given above involves the use of chromic acid mixture, but, owing to a change in the concentration of sulfuric acid, the time of reaction is greatly shortened and the preparation is thus considerably improved.

[1] Ber. 8, 528, 536 (1875).
[2] Ann. **127**, 137 (1863); **128**, 257 (1863).
[3] Ann. **139**, 335 (1866).
[4] J. Am. Chem. Soc. **41**, 1575 (1919).
[5] D. R. P. 117,129; Frdl. **6**, 112.

# XIV

## *p*-NITROBENZYL CYANIDE

$$C_6H_5CH_2CN + HNO_3 \rightarrow (p)NO_2C_6H_4CH_2CN + H_2O$$

Prepared by G. R. ROBERTSON.
Checked by ROGER ADAMS and H. O. CALVERY.

### 1. Procedure

IN a 2-l. round-bottom flask, fitted with a stopper holding a dropping funnel and a mechanical stirrer, is placed a mixture of 275 cc. of concentrated nitric acid (sp. gr. 1.42) and 275 cc. of concentrated sulfuric acid (sp. gr. 1.84). This is cooled to 10° in a freezing mixture, and 100 g. of benzyl cyanide (free from alcohol and water) are run in slowly, at such a rate that the temperature remains at about 10° and does not exceed 20°. After all the benzyl cyanide has been added (about one hour), the ice bath is removed, the mixture is stirred for an hour and then poured on to 1200 g. of crushed ice. A pasty mass slowly separates; more than half of this mass is *p*-nitrobenzyl cyanide, the other constituents being *o*-nitrobenzyl cyanide, and a variable amount of an oil which resists hydrolysis; apparently no dinitro compounds are formed. The mass is filtered on a porcelain funnel with suction, pressed well to remove as much oil as possible, and dissolved in 500 cc. of boiling alcohol (95 per cent). On cooling, *p*-nitrobenzyl cyanide crystallizes; the mother liquor, on distillation, gives an impure alcohol which can be used for the next run. Recrystallization from 550 cc. of 80 per cent alcohol (sp. gr. 0.86 to 0.87) yields 70 to 75 g. (50–54 per cent) of a product which melts at 115–116°.

This product is satisfactory for most purposes, and incidentally for the preparation of *p*-nitrophenylacetic acid. Occa-

sionally it must be free even from traces of the ortho compound, and in this case should be crystallized again from 80 per cent alcohol; it then melts at 116–117°.

## 2. Notes

Fuming nitric acid may be used in nitrating benzyl cyanide, but the method here described is cheaper.

The yield of 70 g. is obtained from benzyl cyanide, which boils over a 5° range prepared as described in preparation III (p. 9). Very pure benzyl cyanide will give a slightly higher yield, while commercial grades may give only 50 g. of *p*-nitrobenzyl cyanide and much oil.

The reaction has been also carried out with 500 g. of benzyl cyanide. Under these conditions a 5-l. flask was used, and it required two and a half hours to add the benzyl cyanide. The yield of product was 325 to 370 g.

## 3. Other Methods of Preparation

Nitrobenzyl cyanide has hitherto been prepared by the action of fuming nitric acid [1] on benzyl cyanide.

[1] Ber. **17**, 505 (1884); **33**, 170 (1900); J. Biol. Chem. **39**, 585 (1919); J. Am Chem. Soc. **43**, 180 (1921).

# *p*-NITROPHENYLACETIC ACID

$$(p)NO_2C_6H_4CN + H_2SO_4 + 2\ H_2O \rightarrow (p)NO_2C_6H_4CH_2CO_2H + NH_4HSO_4$$

Prepared by G. R. Robertson.
Checked by Roger Adams and H. O. Calvery.

## 1. Procedure

In a 1-l. round-bottom flask are placed 100 g. of *p*-nitrobenzyl cyanide. A solution of 300 cc. of concentrated sulfuric acid (sp. gr. 1.84) in 280 cc. of water is prepared, and two-thirds of this solution is poured on to the *p*-nitrobenzyl cyanide. The mixture is shaken well, until the solid is all moistened with the acid. Any solid material sticking to the walls of the vessel is now washed down into the liquid with the remainder of the acid, the flask is attached to a reflux condenser, then set, without shaking, over a 10-cm. hole in a large sheet of asbestos board which rests on a tripod, and heated until the mixture boils. The boiling is continued for fifteen minutes.

The reaction mixture, which becomes rather dark, is diluted with an equal volume of cold water and cooled to 0° or below. The solution is filtered, the precipitate is washed several times with ice water and then dissolved in 1600 cc. of boiling water. (A few grams of animal charcoal are added in dissolving the precipitate, if a technical *p*-nitrobenzyl cyanide has been used.) This solution is filtered as rapidly as possible through a large folded filter, preferably with a steam funnel. In spite of all precautions, however, some solid usually separates on the filter. This must be redissolved in a minimum quantity of boiling water, and this solution then filtered into the main solution. The

*p*-nitrophenylacetic acid separates in long, pale-yellow needles, which melt at 151–152°. The yield is 103 to 106 g. (92–93 per cent of the theoretical amount).

## 2. Notes

If the flask is not protected with an asbestos board or the equivalent, decomposition occurs where the substance is superheated on the side walls of the flask. If crystals of the cyanide are allowed to remain on the upper walls of the flask, they are not easily washed down and so are not hydrolyzed.

The solubility curve of *p*-nitrophenylacetic acid is very steep at temperatures near 100°, so that the filtering of the boiling solution should be rapid.

If a good grade of cyanide be used, it is not necessary to add bone-black in order to obtain the acid in a pure state.

In making experiments with 500 g. of *p*-nitrobenzyl cyanide, it was found that the time for hydrolysis was about the same as when smaller amounts were used.

## 3. Other Methods of Preparation

*p*-Nitrophenylacetic acid has been formed by the nitration of phenylacetic acid;[1] by the hydrolysis of its ester [2] or its amid;[3] and by the hydrolysis of its nitrile with hydrochloric acid.[4]

[1] Ber. **42**, 3596 (1909).
[2] Ber. **12**, 1765 (1879).
[3] Ber. **14**, 2342 (1881).
[4] Ber. **15**, 834 (1882).

# XVI

## NITROSO-β-NAPHTHOL

$$C_{10}H_7OH(\beta) + HNO_2 \rightarrow C_{10}H_6(OH)NO(1, 2) + H_2O$$

Prepared by C. S. Marvel and P. K. Porter.
Checked by H. T. Clarke and W. W. Hartman.

### 1. Procedure

In a 12-l. round-bottom flask fitted with a mechanical stirrer are placed 500 g. of technical β-naphthol dissolved in a warm solution of 140 g. of sodium hydroxide in 6 l. of water. The solution is cooled to 0° in an ice-and-salt bath, and 250 g. of powdered technical sodium nitrite is added. Stirring is started and 1100 g. of sulfuric acid (sp. gr. 1.32) are added from a dropping funnel, at such a rate that the whole is added in one to one and a half hours, the temperature being kept at 0°. During the reaction crushed ice is added from time to time to maintain the temperature at 0°; about 1 kg. is usually used. After all of the sulfuric acid has been added, the solution should react acid to Congo paper. The mixture is stirred one hour longer at the low temperature and then the nitroso-β-naphthol, which has gradually separated out during the reaction, is filtered with suction and washed thoroughly with water. The product is at first light yellow in color, but after three to four days it gradually changes to a dark brown. The moisture content seems to have some effect on the color. After the product has been air-dried for about four days, the yield is about 665 g.; it melts at 97°. A sample of this partially dried product, on drying *in vacuo* over sulfuric acid for twenty hours, loses about 10 per cent of its weight and the melting point is 106°. By longer drying under ordinary conditions, the melting point of 106° is

reached. The total yield of dry product is about 595 g. (99 per cent of the theoretical amount).

This product is satisfactory for all purposes. It may be obtained in a crystalline condition, however, by recrystallizing from hot ligroin (sp. gr. 0.71–0.72). About 2 g. of nitroso-β-naphthol will dissolve in 15 cc. of boiling ligroin. The product is not very soluble in cold ligroin, so that nearly all is recovered

## 2. Notes

It is very necessary to keep the temperature near 0° while adding the sulfuric acid, or a tarry product will be obtained. Vigorous stirring and the addition of the sulfuric acid at the proper rate are essential for a good product.

A large vessel is needed for the reaction, as the nitroso-β-naphthol separates in a finely divided condition and there is some tendency to foam.

The final air-dried product is pure except for its moisture content, as is shown by the fact that on drying *in vacuo* it has a very good melting point. A sample of Kahlbaum's nitroso-β-naphthol melted at 101–105°.

## 3. Other Methods of Preparation

Nitroso-β-naphthol has been made by the action of hydroxylamine hydrochloride on β-naphtho-quinone-chlorimide;[1] by the action of sulfuric acid upon a solution of potassium or sodium nitrite and the sodium salt of β-naphthol;[2] by the action of sodium nitrite upon an alcoholic solution of zinc chloride and β-naphthol;[3] by the action of sodium nitrite upon β-naphthol suspended in zinc sulfate solution;[4] by the action of nitrous acid on β-dinaphthol methane;[5] and by the action of nitrosyl sulfate upon the sodium salt of β-naphthol.[6]

[1] Ber. **27**, 241 (1894).
[2] Ber. 8, 1026 (1875); **27**, 3076 (1894); J. Chem. Soc. **45**, 295 (1884).
[3] Ber. **18**, 705 (1885).
[4] D. R. P. 25,469; Frdl. **1**, 335 (1883).
[5] Ber. **33**, 806 (1900).
[6] J. Chem. Soc. **32**, 47 (1877); Ann. **189**, 146 (1877).

# XVII

## PHENYLACETIC ACID

$$C_6H_5CH_2CN + 2\ H_2O + H_2SO_4 \rightarrow C_6H_5CH_2CO_2H + NH_4HSO_4$$

Prepared by ROGER ADAMS and A. F. THAL.
Checked by O. KAMM and A. O. MATTHEWS.

### 1. Procedure

IN a 5-l. round-bottom flask, fitted with a mechanical stirrer and reflux condenser, are mixed 1150 cc. of water, 840 cc. of commercial sulfuric acid and 700 g. of benzyl cyanide (preparation III, p. 9). The mixture is heated under a reflux condenser and stirred for three hours, cooled slightly and then poured into 2 l. of cold water. The mixture should be stirred so that a solid cake is not formed; the phenylacetic acid is then filtered off. This crude material should be melted under water and washed by decantation several times with hot water. These washings, on cooling, deposit a small amount of phenylacetic acid which is filtered off and added to the main portion of material. The last of the hot water is poured off from the material while it is still molten and it is then transferred to a 2-l. Claisen distilling flask and distilled *in vacuo*. A small amount of water comes over first and is rejected; about 20 cc., containing an appreciable amount of benzyl cyanide, then distils. This fraction is used in the next run. The distillate boiling 176–189°/50 mm. is collected separately and solidifies on standing. It is practically pure phenylacetic acid, m. p. 76–76.5°; it amounts to 630 g. (77.5 per cent of the theoretical amount). As the fraction which is returned to the second run of material contains a considerable portion of phenylacetic acid, the yield actually amounts to at least 80 per cent.

For the preparation of small quantities of phenylacetic acid, it is convenient to use the modified method given in the Notes.

## 2. Notes

The standard directions for the preparation of phenylacetic acid specify that the benzyl cyanide is to be treated with dilute sulfuric acid prepared by adding three volumes of sulfuric acid to two volumes of water. There action, however, goes so vigorously that it is always necessary to have a trap for collecting the benzyl cyanide which is blown out of the apparatus. The use of the more dilute acid, as described in the above directions, is more satisfactory.

The phenylacetic acid may also be made by boiling under a reflux condenser for eight to fifteen hours, without a stirrer, but this method is not nearly so satisfactory as that described in the procedure.

When only small quantities of the acid are required, the following modified procedure is of value. One hundred grams of benzyl cyanide are added to a mixture containing 100 cc. of water, 100 cc. of concentrated sulfuric acid, and 100 cc. of glacial acetic acid. After this has been heated for forty-five minutes under a reflux condenser, the hydrolysis is practically complete. The reaction mixture is then poured into water, and the phenylacetic acid isolated in the usual manner.

The odor of phenylacetic acid is disagreeable and persistent.

## 3. Other Methods of Preparation

The standard method of preparation of phenylacetic acid is by the hydrolysis of benzyl cyanide with either alkali [1] or acid.[2] The acid hydrolysis runs by far the more smoothly and so was the only one studied. There are numerous other ways in which phenylacetic acid has been formed, but none of them is of practical importance for its preparation. These methods include the following: the action of water on phenyl ketene;[3] the

[1] Ann. **96**, 247 (1855); Ber. **14**, 1645 (1881); Compt. rend. **151**, 236 (1910).

[2] Ber. **19**, 1950 (1886).

[3] Ber. **44**, 537 (1911).

hydrolysis and subsequent oxidation of the product between benzaldehyde and hippuric acid;[1] the reduction of mandelic acid;[2] the reduction of benzoylformic acid with hydriodic acid and phosphorus;[3] the hydrolysis of benzyl glyoxalidone;[4] the fusion of atropic acid with potassium hydroxide;[5] the action of alcoholic potash upon chlorophenylacetylene;[6] the action of benzoyl peroxide upon phenylacetylene;[7] the alkaline hydrolysis of triphenylphloroglucinol;[8] the action of ammonium sulfide upon acetophenone;[9] the heating of phenylmalonic acid;[10] the hydrolysis of phenylacetoacetic ester;[11] the action of hydriodic acid upon mandelonitrile.[12]

[1] Ann. **370**, 371 (1909).
[2] Z. Chem. (2) **1**, 443 (1865); Ber. **14**, 239 (1881).
[3] Ber. **10**, 847 (1877).
[4] J. prakt. Chem. (2) **82**, 52, 58 (1910).
[5] Ann. **148**, 242 (1868).
[6] Ann. **308**, 318 (1899).
[7] J. Russ. Phys. Chem. Soc. **42**, 1387 (1910); Chem. Zentr. **1911** (I) 1279.
[8] Ann. **378**, 263 (1911).
[9] Ber. **21**, 534 (1888); J. prakt. Chem. (2) **81**, 384 (1910).
[10] Ber. **27**, 1094 (1894).
[11] Ber. **31**, 3163 (1898).
[12] Inaugural Dissertation of A. Kohler (1909), Univ. of Bern.

# XVIII

## PHENYLACETYLENE

$$C_6H_5CH{=}CHBr + KOH \rightarrow C_6H_5C{\equiv}CH + KBr + H_2O$$

Prepared by JOHN C. HESSLER.
Checked by J. B. CONANT and E. R. BARRETT.

### 1. Procedure

IN a 500-cc. Pyrex distilling flask are placed 150 g. of potassium hydroxide. The mouth of the flask is provided with a one-hole stopper holding a dropping funnel; the side tube of the flask is connected with a condenser set for downward distillation. The $\beta$-bromostyrene (100 g.) is placed in the dropping funnel.

The distilling flask is gradually heated in an oil bath until the temperature of the bath is 200°, and the bromostyrene is then dropped in upon the molten potassium hydroxide, at the rate of somewhat less than a drop a second. Since the boiling point of phenylacetylene is 142–143°, and that of bromostyrene is 218-220°, the phenylacetylene distils away from the unchanged bromostyrene.

While the bromostyrene is being dropped in, the temperature of the oil bath is raised very gradually to 215–220°, and is kept at this temperature until all the bromostyrene has been added. Finally the temperature is raised to 230°, and is held there until no more distillate comes over. The distillate is colorless; it consists of two layers, the lower one being water. The upper layer is separated and dried with solid potassium hydroxide. It is then distilled. The yield of the distilled phenylacetylene, boiling at 142–144°, is 37 g. (67 per cent of the theoretical amount).

## 2. Notes

Toward the end of the reaction, a crust of potassium bromide may tend to cover the melted potassium hydroxide. One can break the crust by shaking the distilling flask gently, or by using a glass rod inserted through a second hole in the stopper holding the dropping funnel.

It is convenient to have such a rod or stirrer passing through a mercury seal in the stopper of the flask. An occasional turn of this stirrer breaks the crust and facilitates the operation. Mechanical stirring should not be employed, as it reduces the yield tremendously. Apparently this is because it facilitates the solution of bromostyrene in the tarry by-products and thus causes it to polymerize instead of reacting with the potassium hydroxide. A single Pyrex flask can be used for only three or four runs. The flask should be emptied while still very hot.

The yield of material can be somewhat increased by working with small lots (25 g. of bromostyrene).

The use of steel or copper vessels in place of a glass flask seems to diminish the yield slightly.

## 3. Other Methods of Preparation

Phenylacetylene has been prepared by the elimination of carbon dioxide from phenylpropiolic acid by means of phenol[1] or aniline[2] or by heating with barium hydroxide;[3] from styrene dibromide, by heating with potassium hydroxide in alcohol;[4] by heating β-bromo or chloro styrene with sodium ethylate or potassium hydroxide in alcohol;[5] by passing the vapors of α-dichloroethylbenzene over hot soda lime;[6] by the action of alcoholic potassium hydroxide on dibenzal-acetone tetra-

[1] Ber. **20**, 3081 (1887).

[2] Rec. trav. chim. **15**, 157 (1896).

[3] Ann. **221**, 70 (1883).

[4] Ann. **154**, 155 (1870); **235**, 13 (1886); Bull. soc. chim. **35**, 55 (1881); (3) **25**, 309 (1901).

[5] Ann. **308**, 265 (1899); **342**, 220 (1905).

[6] Jahresb. **1876**, 398; Gazz. chim. ital. **22** (2), 67 (1892); Bull. soc. chim. (3) **25**, 309 (1901).

bromide;[1] by the action of aqueous potassium hydroxide on phenyl propargylaldehyde;[2] by the action of molten potassium hydroxide on $\beta$-bromo-styrene.[3]

[1] Ber. **39**, 4146 (1906).
[2] Ber. **31**, 1023 (1898).
[3] J. Am. Chem. Soc. **44**, 425 (1922).

XIX

## PHENYLHYDRAZINE

$$C_6H_5NH_2 \cdot HCl + NaNO_2 + HCl \rightarrow C_6H_5N_2Cl + NaCl + 2\,H_2O$$

$$C_6H_5N_2Cl + 4H(Na_2SO_3) \rightarrow C_6H_5NHNH_2 \cdot HCl$$

Prepared by G. H. COLEMAN.
Checked by J. B. CONANT and H. R. THOMPSON.

### 1. Procedure

IN a 12-l. round-bottom flask, fitted with a mechanical stirrer, are placed 1045 cc. of concentrated commercial hydrochloric acid (sp. gr. 1.138). The flask is surrounded with a freezing mixture of ice and salt, and when the contents are at 0°, stirring is started and 500 g. of cracked ice are added; then 372 g. of aniline, also cooled to 0°, are run in during five minutes. The mixture is treated with 500 g. more of cracked ice, and a cold solution (0°) of 290 g. of technical sodium nitrite dissolved in 600 cc. of water are allowed to run in slowly (twenty to thirty minutes) from a dropping funnel, the end of which is drawn to a small tip, and reaches nearly to the bottom of the flask. During this addition, the stirrer is operated rather vigorously, and the temperature is kept as near 0° as possible by the frequent addition of cracked ice (about 1 kg).

In the meantime, a sodium sulfite solution is prepared by dissolving 890 g. of sodium hydroxide, of about 90 per cent purity, in about 1 l. of water and then diluting to 6 l. A few drops of phenolphthalein solution are added and sulfur dioxide passed in, first until an acid reaction is indicated and then for two or three minutes longer. During the addition of the sulfur dioxide, the solution is cooled with running water. On account of the strong alkaline solution, the original color produced by

the phenolphthalein is very faint, but this slowly increases until it becomes deep just before the acid point is reached. It is best to remove a small sample of the liquid from time to time, dilute with three or four volumes of water and add a drop more of phenolphthalein.

The sodium sulfite solution is placed in a 12-l. flask and cooled to about 5°. Approximately 500 g. of cracked ice are added, and then, with mechanical stirring, the diazonium salt solution is run in as rapidly as possible. The mixture becomes a bright orange-red. The flask is now warmed to about 20° on a steam bath, until the solid sodium sulfite, which has separated while cooling, redissolves. The total amount of liquid is now about 10 l. One-half of this is poured into another 12-l. flask, and both halves are warmed on the steam bath to 60–70°, until the color becomes quite dark (thirty to sixty minutes). Sufficient hydrochloric acid (300–400 cc.) is now added to each flask to make the solutions acid to litmus. The heating is continued and the color gradually becomes lighter until, after four to six hours, the solutions have become nearly colorless; they may be heated overnight, if desired.

To the hot solutions are now added about one-third of their volume of concentrated hydrochloric acid (2 l. to each portion) and the mixtures cooled, first in running water, then in a freezing mixture, to 0°. The phenylhydrazine hydrochloride precipitates in the form of slightly yellowish or pinkish crystals which may be filtered off and dried.

The free base is liberated by adding to the phenylhydrazine hydrochloride 1 l. of a 25 per cent solution of sodium hydroxide. The phenylhydrazine separates and is taken up with benzene (two 300-cc. portions). The combined extractions are well dried with 200 g. of solid sodium hydroxide, poured off, and distilled. Most of the benzene may be distilled under ordinary pressure, and the remainder, and any low-boiling impurities, under diminished pressure. The pure phenylhydrazine boils at 137–138°/18 mm., and is obtained as a pale-yellow liquid. It can be crystallized on cooling in an ice bath; the crystals melt at 23°. The crude phenylhydrazine from two lots of aniline

(744 g.) is best distilled at one time and gives 695–725 g. of pure product (80–84 per cent of the theoretical amount).

## 2. Notes

If the sodium sulfite solution contains an excess of alkali, a black tar tends to form when the solution is warmed, and very little phenylhydrazine is obtained. Great care must be taken in determining the end point in the neutralization of the sodium hydroxide by the sulfur dioxide.

If the sodium sulfite-diazonium salt mixture is acidified before warming or before becoming dark, the red color of the solution does not disappear on heating, and the precipitated phenylhydrazine hydrochloride obtained is colored red.

The benzene solution of phenylhydrazine should be well dried before distilling, since the presence of moisture causes an increased amount of foaming to take place just after the benzene has distilled off. When the distillation is carried out carefully, practically no phenylhydrazine distils with the benzene or other low-boiling impurities.

In order to obtain the maximum yield, it is necessary to cool the hydrochloric acid solution of the phenylhydrazine hydrochloride from 20° to 0°, before filtration. From 5 to 10 per cent of product separates between these two temperatures. When this is done, no more phenylhydrazine hydrochloride is obtained by concentration of the mother liquor. An increase in the amount of hydrochloric acid above 2 l. for the precipitation of the hydrochloride produces no increase in yield of product.

Most published directions for the preparation of phenylhydrazine specify the use of zinc dust and acetic acid following the reduction with sodium sulfite. No improvement in the quality or quantity of the product was obtained by using zinc and acetic acid.

It is best to use freshly prepared sodium sulfite for the reduction, since the commercial quality is poor and gives a lower yield of phenylhydrazine. A cylinder of liquid sulfur dioxide should, of course, be available.

The rapid addition of the diazonium salt solution to the sodium sulfite seems to be advantageous.

Pure phenylhydrazine dissolves in dilute acetic acid to yield a perfectly clear solution.

The phenylhydrazine hydrochloride may be purified by crystallizing from water. A 600-cc. portion of water is used for 100 g. of crude hydrochloride, and the solution boiled a short time with a few grams of animal charcoal. After filtering, 200 cc. of concentrated hydrochloric acid are added, and the mixture cooled to 0°. Pure white crystals in a yield of 85–90 g. are obtained.

Rubber gloves should be worn when working with large quantities of phenylhydrazine, since the product may cause serious injury to the skin. The vapors of phenylhydrazine should not be inhaled.

### 3. Other Methods of Preparation

Phenylhydrazine has been prepared by the reduction of benzene diazonium salts with sulfites;[1] by the reduction of benzene diazonium chloride with stannous chloride;[2] by the reduction of benzene diazonium hydrate with zinc or sulfur dioxide;[3] by the reduction of sodium benzene diazotate with sodium stannite;[4] by the reduction of diazoamino benzene;[5] by the reduction of nitrosophenyl hydroxylamine or its methyl ether;[6] and by the action of hydrazine hydrate on phenol.[7]

The most feasible method consists in the reduction of diazonium salts with sodium sulfite. Although this method is given in several laboratory manuals, the results were not found entirely satisfactory. The present directions provide for a lengthy but essential heating of the diazonium-sulfite mixture, omit the useless zinc dust reduction, and supply exact details for preparation on a fairly large laboratory scale.

[1] Ann. **190**, 79 (1878); Ber. **20**, 2463 (1887).
[2] Ber. **16**, 2976 (1883); **17**, 572, footnote (1884).
[3] Ber. **31**, 346 (1898).
[4] Ber. **36**, 816 (1903).
[5] Ann. **190**, 77 (1878).
[6] Ber. **31**, 582 (1898).
[7] Ber. **31**, 2910 (1898).

# XX

## PHTHALIMIDE

$$C_6H_4\left\langle\begin{matrix}CO\\ CO\end{matrix}\right\rangle O + NH_4OH \rightarrow C_6H_4\left\langle\begin{matrix}CO\\ CO\end{matrix}\right\rangle NH + 2H_2O$$

$$2C_6H_4\left\langle\begin{matrix}CO\\ CO\end{matrix}\right\rangle O + (NH_4)_2CO_3 \rightarrow 2C_6H_4\left\langle\begin{matrix}CO\\ CO\end{matrix}\right\rangle NH + CO_2 + 3H_2O$$

Prepared by W. A. NOYES and P. K. PORTER.
Checked by H. T. CLARKE and J. H. BISHOP.

### 1. Procedure

IN a 5-l. round-bottom flask (Pyrex) is placed a mixture of 500 g. of phthalic anhydride and 400 g. of 28 per cent ammonium hydroxide. The flask is fitted with an air condenser not less than 10 mm. in diameter and is then slowly heated with a free flame until the mixture is in a state of quiet fusion at a temperature of about 300°. It requires about one hour before all the water has gone and about one and a half to two hours before the temperature of the reaction mixture reaches 300° and the mixture is a homogeneous melt. It is advisable, during the heating, to shake the flask occasionally; some material sublimes into the condenser and must be pushed down with a glass rod. The hot reaction mixture is now poured out into a crock, covered with a paper to prevent loss by sublimation, and allowed to cool. The product is practically pure without further treatment, and melts at 232–235°. The yield is 470–480 g. (94–95 per cent of the theoretical amount).

Phthalimide may also be made by using 500 g. of phthalic anhydride and 500 g. of ammonium carbonate which has been previously ground in a mortar. The subsequent procedure is

the same as when aqueous ammonia is used. Frequent shaking is necessary, and the sublimed material must be occasionally pushed back into the reaction flask. About two hours are required for completion.

## 2. Notes

Several smaller runs of 25 g. of phthalic anhydride gave the same percentage yield.

Phthalimide may be recrystallized from water, but only about 4 g. of phthalimide will dissolve in a liter of boiling water. It may also be crystallized from alcohol, in which solvent it dissolves to the extent of five parts in a hundred at boiling temperature.

On a large scale, it would be advisable to collect the small amount of ammonia given off during the reaction.

If desired, the product obtained by pouring the reaction mass into the crock may be treated with hot water to soften the cake, broken up with a glass rod, transferred to a flask and boiled with water for a few minutes. This treatment, however, is quite unnecessary; for all practical purposes, the crude cake, as it is obtained, may be ground up and used directly.

## 3. Other Methods of Preparation

Phthalimide has been formed by heating ammonium phthalate;[1] by heating acid ammonium phthalate;[2] by passing dry ammonia over heated phthalic anhydride;[3] by treating phthalyl chloride with dry ammonia;[4] by heating phthalamide;[5] by heating phthalic anhydride with ammonium thiocyanate;[6] by heating phthalic anhydride with urea;[7] by heating phthalic

[1] Jahresb. **1868**, 549; Ann. **19**, 47 (1836); **41**, 110 (1842); **42**, 220 (1842); **205**, 300 (1880); **215**, 181 (1882).

[2] Jahresb. **1847–1848**, 590.

[3] Am. Chem. J. **3**, 29 (1881).

[4] Am. Chem. J. **3**, 28 (1881).

[5] Ber. **39**, 2278 (1906).

[6] Ber. **19**, 1398 (1886),

[7] Ber. **10**, 1166 (1877); Am. Chem. J. **18**, 333 (1896); J. Am. Chem. Soc. **32**, 116 (1910); Z. angew. Chem. **32**, I, 301 (1919).

anhydride with ammonium carbonate;[1] by heating phthalic acid with nitriles;[2] by fusing *o*-cyanobenzoic acid;[3] and by the action of potash on *o*-cyanobenzaldehyde.[4]

Of these, the first three are the only ones which need be considered as methods for the preparation of phthalimide. It was found that the third was by no means easy to bring about: dry phthalic anhydride is apparently only superficially affected by the dry ammonia, and it was difficult to introduce sufficient heat into the loose mass of crystals to cause the reaction to start.

[1] J. Am. Chem. Soc. **42**, 1282 (1920).

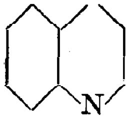
[2] J. Am. Chem. Soc. **18**, 680 (1896); **20**, 654 (1898).

[3] Rec. trav. chim. (1) **11**, 93 (1892).

[4] Ber. **30**, 1698 (1897).

## XXI

## QUINOLINE

$C_3H_5(OH)_3 + C_6H_5NH_2 + 4O(C_6H_5NO_2) \rightarrow$  $+ 4H_2O$

Prepared by H. T. Clarke and Anne W. Davis.
Checked by Roger Adams and A. W. Sloan.

### 1. Procedure

In a 5-l. round-bottom flask, fitted with an efficient reflux condenser of wide bore, are placed, in the following order, 80 g. of powdered crystalline ferrous sulfate, 865 g. of glycerol (c. p.), 218 g. of aniline, 170 g. of nitrobenzene, and 400 cc. of concentrated sulfuric acid (sp. gr. 1.84). The contents of the flask are well mixed and the mixture heated gently over a free flame. As soon as the liquid begins to boil, the flame is removed, since the heat evolved by the reaction is sufficient to keep the mixture boiling for one-half to one hour. If the reaction proceeds too violently at the beginning, the reflux condenser may be assisted by placing a wet towel over the upper part of the flask. When the boiling has ceased the heat is again applied and the mixture boiled for five hours. It is then allowed to cool to about 100° and transferred to a 12-l. flask; the 5-l. flask is rinsed out with a small quantity of water. The 12-l. flask is then connected with the steam-distillation apparatus shown in Fig. 3, a 12-l. flask being used as a receiver; steam is passed in (without external heat) until 1500 cc. have distilled (ten to thirty minutes). This removes all the unchanged nitrobenzene (10–20 cc.). The current of steam is then interrupted, the receiver is changed, and 1500 g. of 40 per cent sodium hydroxide solution are added cautiously through the steam inlet. The heat of neutrali-

zation is sufficient to cause the liquids to boil and thus become thoroughly mixed. Steam is then passed in as rapidly as possible until all the quinoline has distilled. In this process, 6–8 l. of distillate are collected (two and a half to three and a half hours are required, unless a very efficient condensing apparatus is used, under which conditions the distillation may be complete in one-half to one and a half hours). The distillate is allowed to cool, and the crude quinoline separated. The aqueous layer of the distillate is again distilled with steam

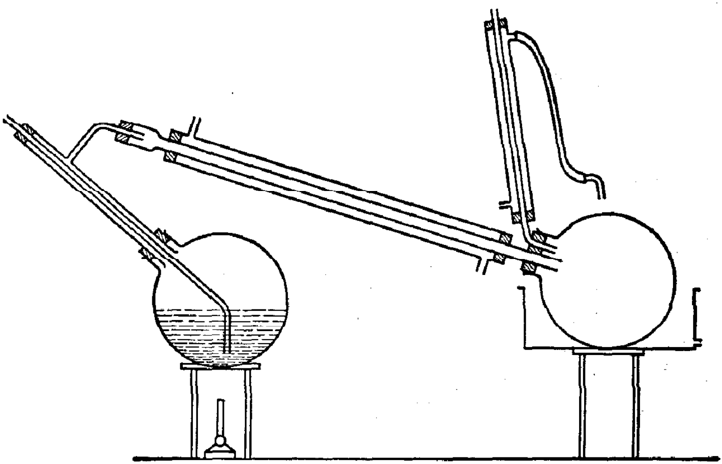


FIG. 3.

until all the quinoline has been volatilized and collected in about 3 l. of distillate.

These 3 l. of distillate are then mixed with the first yield of quinoline and 280 g. (150 cc.) of concentrated sulfuric acid are added. The solution is cooled to 0–5°, and a saturated solution of sodium nitrite added until a distinct excess of nitrous acid is present (as shown either by starch-potassium iodide paper or by the odor). This generally requires 50 to 70 g. of sodium nitrite. The mixture is then warmed on a steam bath for an hour, or until active evolution of gas ceases, and is then distilled with steam until all the volatile material has been expelled (4 l. of

distillate will result). The receiver is then changed and the mixture in the distillation flask is neutralized, as before, with 700 g. of 40 per cent sodium hydroxide solution. The quinoline is distilled exactly as described above, the aqueous portions of the distillate being distilled with steam until all the quinoline has been isolated. The crude product is then distilled under reduced pressure, and the fraction which boils at 110–114°/14 mm. is collected. The foreruns are separated from any water which may be present, dried with a little solid alkali, and redistilled. The total yield is 255–275 g. (84–91 per cent of the theoretical amount based on the aniline taken).

## 2. Notes

Although these directions have been used many times with results exactly as described, in a few cases the yields have dropped to 60–65 per cent without any apparent reason. At present no explanation can be given for this.

In the Skraup synthesis of quinoline the principal difficulty has always been the violence with which the reaction generally takes place; it occasionally proceeds relatively smoothly, but in the majority of cases gets beyond control, with consequent loss of material through the condenser. By the addition of ferrous sulfate, which undoubtedly functions as an oxygen carrier, the reaction is extended over a longer period of time. It is thus possible to work with much larger quantities of material when ferrous sulfate is employed.

It is important that the materials should be added in the correct order; should the sulfuric acid be added before the ferrous sulfate, the reaction may start at once. It is also important to mix the materials well before applying heat; the aniline sulfate should have dissolved almost completely and the ferrous sulfate should be distributed throughout the solution. To avoid danger of overheating, it is well to apply the flame away from the center of the flask where any solids would be liable to congregate.

In the apparatus for steam distillation, the greater portion of the condensation is effected by the stream of water passing over

the receiver. It is, therefore, necessary that the stream passing through the condenser should be sufficiently rapid to cause it to form a uniform film over the receiving flask. A 12-l. flask is even more efficient as a condenser than the 5-l. flask. It is important that the tube through which the vapors leave the distillation flask should be neither too short nor, especially, too narrow. Where the external diameter of the steam inlet tube is 5–8 mm., the internal diameter of this steam head should be not less than 28 mm. Were it less, the current of steam passing through it would be so rapid as to prevent small quantities of liquid from returning to the flask, and these would be driven over into the receiver.

Much time can be saved by the use of the steam distillation apparatus described, especially when large quantities have to be handled. The above directions avoid the use of extraction methods, which not only consume more time but may lead to appreciable losses of material. If the downward condenser is of iron, the apparatus is even more efficient and the time for the steam distillation is halved.

The percentage yields have been based on the amount of aniline taken. It would probably be more legitimate to base the calculation on the amounts of aniline taken and of nitrobenzene not recovered, since undoubtedly the latter is reduced to aniline during the course of the reaction. If this be done, the yield is found to be only 55 to 60 per cent of the calculated amount.

In a number of experiments, the glycerol used contained an appreciable amount of water. Under these conditions, the yield of product is much lower. "Dynamite" glycerol containing less than half a per cent of water is best employed; U. S. P. glycerol contains 5 per cent of water and usually gives lower yields.

### 3. Other Methods of Preparation

Quinoline has been produced by passing the vapor of allylaniline over red-hot lead oxide;[1] by heating acrylideneaniline, or better, a mixture of aniline, glycerol and sulfuric acid;[2] by

[1] Ber. **12**, 453 (1879).
[2] Ber. **13**, 911 (1880); Monatsh. **1**, 316 (1880).

heating aniline with glycerol and sulfuric acid, using nitrobenzene as an oxidizing agent;[1] by treating a mixture of glyoxal and *o*-toluidine with alkali;[2] by treating a solution of *o*-aminobenzaldehyde with acetaldehyde and alkali;[3] by heating methylacetanilide with zinc chloride;[4] by heating aminoazobenzene with glycerol and sulfuric acid;[5] by heating a mixture of aniline, glycerol and sulfuric acid with arsenic acid.[6]

Of the above methods, the only ones which need be considered are those in which a mixture of aniline, glycerol and sulfuric acid is heated with an oxidizing agent. With the use of nitrobenzene, the reaction, according to the original method, takes place with extreme violence.

The method above described is the most satisfactory for the preparation of quinoline itself, but for the preparation of homologues of quinoline, the use of arsenic acid is preferable, since the yields are somewhat greater.

Since the work was carried out, a method has been published[7] in which aniline, glycerol and sulfuric acid are treated with ferric oxide. By this method Adams and Parks were unable to obtain yields comparable with those resulting from the above directions.

[1] Monatsh. **2**, 141 (1881); J. prakt. Chem. (2) **49**, 549 (1894).
[2] Monatsh. **15**, 277 (1894).
[3] Ber. **15**, 2574 (1882); **16**, 1833 (1883).
[4] Ber. **23**, 1903 (1890).
[5] Ber. **24**, 2623 (1891).
[6] Ber. **29**, 704 (1896).
[7] Chem. News **121**, 205 (1920).

# XXII

## QUINONE

$$(1)HOC_6H_4OH(4)+O(Na_2Cr_2O_7+H_2SO_4) \rightarrow O=C_6H_4=O+H_2O$$

Prepared by E. B. VLIET.
Checked by ROGER ADAMS and E. E. DREGER.

### 1. Procedure

IN a 2.5-l. beaker, 100 g. of hydroquinone are dissolved in 2000 cc. of water heated to about 50°. After the solid is completely dissolved, the solution is cooled to 20°, 100 g. of concentrated sulfuric acid are slowly poured in, and the mixture is again cooled to 20°. A concentrated solution of technical sodium dichromate is prepared by dissolving 140 g. in 65 cc. of water. This solution is then added gradually to the hydroquinone solution, with the use of a mechanical stirrer (see notes), the mixture being cooled so that the temperature never rises above 30°. At first a greenish-black precipitate forms, but upon further addition of the sodium dichromate solution, the color changes to yellowish green. As soon as this color remains permanent (a slight excess of sodium dichromate does no harm) the reaction is complete. This requires about one-half to three-quarters of an hour; 90 to 110 cc. of sodium dichromate solution is necessary. The mixture is then cooled to about 10° and filtered with suction. As much water as possible is pressed out of the crystals.

The filtrate is extracted twice, 150 cc. of benzene being used for each extraction. The precipitate of quinone is transferred to a 1-l. beaker, and 500 cc. of benzene, including the 300 cc. used to extract the filtrate, are added. The mixture is now

heated with stirring on a steam-bath, and as soon as most of the quinone has dissolved the benzene layer is decanted into another beaker. It is dried while hot by stirring a short time with a little calcium chloride, and then filtered through an ordinary funnel into a 1-l. distilling flask before it cools. There is a certain amount of quinone which does not go into the 500 cc. of benzene, so that the residue is extracted a second time with about 100 cc. of benzene, which is dried and filtered with the first extract. During these extractions, the benzene should not be at the boiling point, as this will cause a considerable volatilization of the quinone.

The distilling flask is now attached to a condenser set for downward distillation, and the benzene is distilled. As soon as the quinone starts to separate, the residue in the flask is transferred to a beaker and cooled in an ice bath. The precipitate is filtered off with suction and the product spread out for a short time to dry. The product is yellow in color and weighs 75 to 80 g. (76–81 per cent of the theoretical amount). Material made in this way will hold its yellow color over long periods of time, provided it is protected from light.

The benzene distillate is yellow and contains some quinone. This, as well as the benzene from the final filtration of the quinone crystals, may be used in a subsequent run and thus raises the yield of the subsequent runs to about 85–90 g. (85–90 per cent of the theoretical amount).

## 2. Notes

As the mixture becomes thick during the oxidation, it is very necessary to use a stirrer which will keep the whole mass agitated by reaching to the sides and bottom of the beaker.

If impure hydroquinone is used, a black, sticky precipitate will usually appear after the addition of the sulfuric acid to the hydroquinone solution. This should be removed, before the oxidation is started, by filtration without suction through a fluted filter.

When technical sodium dichromate is used, the solution

should be filtered with suction, before it is added to the hydroquinone, in order to remove any insoluble impurities.

In the laboratory it is convenient to make several small runs of the size indicated, as far as the oxidation is concerned; but the benzene extractions can be combined.

It is also possible to obtain good yields of quinone in the following manner: 1500 cc. of water, 465 g. of concentrated sulfuric acid and 300 g. of hydroquinone are mixed in a 3-l. beaker. The mixture is cooled to 0°, and 330 g. of sodium dichromate are added in powdered form, the temperature being kept below 5° at all times. This procedure requires a longer time and much more care in the control of conditions than the method described above.

### 3. Other Methods of Preparation

Quinone may be prepared by the oxidation of aniline with dichromate or manganese dioxide and sulfuric acid.[1] This is a more feasible commercial method than the one given. However, the oxidation of hydroquinone is more rapid and convenient and, hence is more desirable for use in the laboratory. Various materials have been oxidized by chemical means to give quinone: they are quinic acid,[2] hydroquinone,[3] benzidine,[4] *p*-phenylenediamine,[5] sulfanilic acid,[6] *p*-phenolsulfonic acid,[7] arbutin,[8] aniline black,[9] and the leaves of various plants.[10] Quinone is also formed by several other methods: by the fermentation of fresh grass;[11] by the action of iodine on the lead salt of hydroquin-

[1] Jahresb. **1863**, 415; Ber. **10**, 1934, 2005 (1877); **16**, 687 (1883); **19**, 1468 (1886); **20**, 2283 (1887); **31**, 1524 (1898); Ann. **200**, 240 (1880); **215**, 127 (1882).

[2] Ann. **27**, 268 (1838).

[3] Ann. **51**, 152 (1844); Am. Chem. J. **14**, 555 (1892).

[4] Jahresb. **1863**, 415.

[5] Jahresb. **1863**, 422.

[6] Ann. **159**, 7 (1871); Ber. **8**, 760 (1875).

[7] Ber. **8**, 760 (1875).

[8] Ann. **107**, 233 (1858).

[9] Ber. **10**, 1934 (1877); **34**, 1285 (1901).

[10] Ann. **89**, 247 (1854); Ber. **34**, 1162 (1901).

[11] Ber. **30**, 1870 (1897).

one;[1] by the decomposition of the compound, $C_6H_4 \cdot 2CrO_2Cl$ with water;[2] by the action of sulfuric acid on phenol blue;[3] by the electrochemical oxidation of aniline,[4] hydroquinone[5] or benzene;[6] by the catalytic oxidation of benzene.[7]

[1] Ber. **31**, 1458 (1898); Am. Chem. J. **26**, 20 (1901).

[2] Ann. chim. phys. (5) **22**, 270 (1881).

[3] Ber. **18**, 2915 (1885); **21**, 889 (1888).

[4] D. R. P. 109,012; Frdl. **5**, 664 (1900); D. R. P. 117,129; Frdl. **6**, 112 (1901); J. Soc. Dyers and Colourists, **36**, 138 (1920).

[5] D. R. P. 117,129; Frdl. **6**, 112 (1901).

[6] D. R. P. 117,251; Frdl. **6**, 109 (1901); U. S. Pat. 1,322,580 (1919); C. A. **14**, 287 (1920); Rev. produits chim. **21**, 219 (1918); **21**, 288 (1918).

[7] U. S. Pat. 1,318,631 (1919); C. A. **14**, 70 (1920).

## XXIII

## SODIUM *p*-TOLUENESULFINATE

$$2\ CH_3C_6H_4SO_2Cl + 3\ Zn \rightarrow (CH_3C_6H_4SO_2)_2Zn + ZnCl_2$$

$$(CH_3C_6H_4SO_2)_2Zn + Na_2CO_3 \rightarrow 2\ CH_3C_6H_4SO_2Na + ZnCO_3$$

Prepared by FRANK C. WHITMORE and FRANCIS H. HAMILTON
Checked by J. B. CONANT and PAUL ALLEN, JR.

### 1. Procedure

FIVE HUNDRED grams of technical *p*-toluenesulfonyl chloride are ground in a mortar to break up all lumps. Three liters of water are placed in a 12-l. crock provided with a large brass stirrer and a tube for passing steam directly into the liquid. Dry steam is passed into the water until the temperature reaches 70°. The steam is then shut off and 400 g. of zinc dust (90 to 100 per cent pure) is added. The sulfonyl chloride is then added in small portions by means of a porcelain spoon. The addition takes about ten minutes. The temperature rises to about 80°. Stirring is continued for ten minutes after the last of the chloride has been added. Steam is then passed into the mixture until the temperature reaches 90°. If it is heated any hotter, bumping takes place. The steam is shut off, and 250 cc. of 12 *N*. sodium hydroxide solution is added. Finely powdered sodium carbonate is then added in 50-g. portions until the mixture is strongly alkaline. The mixture froths considerably, but this causes no trouble unless too small a crock is used. The stirrer is loosened and the crock is removed. The mixture is filtered by suction in a large funnel. The filtrate has a volume of about 4.5 l. The cake of unchanged zinc dust and zinc compounds is transferred to a 3-l. battery jar and placed under the stirrer, and the latter is clamped in place. Water (750 cc.) is added.

the stirrer is started, and steam is passed in until the mixture starts to froth too violently. The steam is then shut off, but the stirring is continued for ten minutes. The mixture is filtered and the filtrate is added to the main solution in a large evaporating dish. The liquid is evaporated over a large burner to a volume of about 1 l., or until a considerable crust forms around the edges. The mixture is then cooled. Large, flat, transparent crystals separate. The thoroughly cooled mixture is filtered by suction, and the crystals are air-dried until efflorescence just starts. They are then bottled. The product is $CH_3C_6H_4SO_2Na \cdot 2H_2O$. Yield 360 g. (64 per cent of the theoretical amount). Careful acidification of the mother liquor with dilute hydrochloric acid yields 15 g. of the free sulfinic acid.

## 2. Notes

The free sulfinic acid may be prepared by dissolving the sodium salt in cold water and carefully acidifying the solution with hydrochloric acid. An excess of the latter must be avoided, as it dissolves the acid to a certain extent. The sulfinic acid is difficult to dry without partial conversion into the sulfonic acid.

## 3. Other Methods of Preparation

Toluenesulfinic acid and its salts have been prepared by three general methods: (1) The reduction of the sulfonyl chloride. The reagents which have been used for this are sodium amalgam,[1] zinc dust in alcohol or water,[2] sodium sulfite,[3] sodium sulfide,[4] potassium hydrosulfide[5] (the thio acid being first formed) and sodium arsenite.[6] (2) From toluene by the Friedel and Crafts reaction, using either sulfur dioxide and hydrogen chloride[7] or sulfuryl chloride.[8] (3) From *p*-toluidine by diazotization and

[1] Ann. **142**, 93 (1867).
[2] Ber. **9**, 1586 (1876).
[3] Ber. **3**, 965 (1870).
[4] D. R. P. 224,019; Chem. Zentr. **1910**, (II), 513
[5] Ber. **42**, 3821 (1909).
[6] Ber. **41**, 3351 (1908); Ber. **42**, 480 (1909).
[7] Ber. **41**, 3318 (1908); J. Chem. Soc. **93**, 754 (1908).
[8] Rec. trav. chim. (2) **30**, 381 (1911).

subsequent treatment with sulfur dioxide and finely divided copper.[1] The compound has also been obtained in certain reactions which, however, would not be suitable for preparative work; thus it is formed by hydrolysis and reduction of certain thio derivatives[2] prepared from the acid itself and also by the decomposition of ditolylsulfonmethylamine.[3]

[1] Ber. **32**, 1141 (1899); J. Chem. Soc. **95**, 344 (1909).

[2] Ber. **15**, 130 (1882); **20**, 2088 (1887); **41**, 3351 (1908).

[3] J. prakt. Chem. (2) **63**, 170 (1901).

# XXIV

## 1, 3, 5-TRINITROBENZENE

$$C_6H_2(NO_2)_3CO_2H \rightarrow C_6H_3(NO_2)_3 + CO_2$$

Prepared by H. T. Clarke and W. W. Hartman.
Checked by J. B. Conant and J. J. Toohy.

### 1. Procedure

The crude trinitrobenzoic acid obtained by oxidation of 360 g. of trinitrotoluene (prep. XXV, p. 95) is mixed with 2 l. of water at 35° in a 5-l. flask provided with a stirrer. Fifteen per cent sodium hydroxide solution is added, with continuous stirring, until a *faint* red color is just produced. (See Notes.) The color is then immediately discharged by means of one or two drops of acetic acid, and the liquid is filtered from unchanged trinitrotoluene. The filtrate is transferred to a 5-l. flask, and 70 cc. of glacial acetic acid are added. The mixture is then gently heated, with continuous stirring, when trinitrobenzene separates in crystalline condition, and floats on the surface of the liquid as a frothy layer. After about one and a half hours the evolution of gas ceases; at this point the crystals begin to stir into the solution. The heating and stirring is continued for three-quarters of an hour, when the mixture is allowed to cool, and the crystals filtered off. A sample of the filtrate should be tested for undecomposed trinitrobenzoic acid: if a precipitate is produced by the addition of sulfuric acid the process must be continued. After recrystallization from glacial acetic acid, the product melts at 121–122°. The yield is 145–155 g. (43 to 46 per cent of the theoretical amount calculated from the trinitrotoluene).

## 2. Notes

During the solution of the trinitrobenzoic acid, the temperature should not be below 35°, owing to the slight solubility of trinitrobenzoic acid in cold water. The heat of neutralization raises the temperature to 45–55°, but the latter temperature should not be exceeded, since any trinitrobenzene formed at this point would later be removed with the unreacted trinitrotoluene.

Care must be taken that no more alkali is added than is just sufficient to produce the faint red color. If an excess of alkali is added it produces a permanent color, which is not removed by acid and colors the final product.

When once the evolution of carbon dioxide sets in, the flame must be cut down so as to avoid the formation of a thick layer of froth which might foam over.

## 3. Other Methods of Preparation

1, 3, 5-Trinitrobenzene can be prepared by heating *m*-dinitrobenzene with nitric acid and sulfuric acid to 120°;[1] by heating 2, 4, 6-trinitrotoluene with fuming nitric acid in a sealed tube at 180° for three hours;[2] by heating 2, 4, 6-trinitrobenzoic acid or its sodium salt with water, alcohol, dilute sodium carbonate or other suitable solvent.[3]

[1] Ber. **9**, 402 (1876); Ann. **215**, 344 (1882).
[2] Ber. **16**, 1596 (1883).
[3] D. R. P. 77,353; Frdl. **4**, 34 (1894).

XXV

## 2, 4, 6-TRINITROBENZOIC ACID

$$C_6H_2(NO_2)_3CH_3 + 3O(Na_2Cr_2O_7 + H_2SO_4) \rightarrow C_6H_2(NO_2)_3CO_2H + H_2O$$

Prepared by H. T. CLARKE and W. W. HARTMAN.
Checked by J. B. CONANT and J. J. TOOHY.

### 1. Procedure

To 3600 g. of concentrated sulfuric acid, in a 5-l. flask placed in an empty water bath, are added 360 g. of technical trinitrotoluene, while the mixture is stirred mechanically. Sodium dichromate ($Na_2Cr_2O_7 \cdot 2\ H_2O$) is now added in small quantities (*precaution*: see Notes), with constant stirring, until the temperature of the mixture reaches 40°; the empty water bath is now filled with cold water and the addition of sodium dichromate continued at such a rate that the temperature remains at 45–55°. In all 540 g. of sodium dichromate are added, the addition taking one to two hours. When all has been added, the mixture, which has now become very thick, is stirred for two hours at 45–55°, and poured into a crock containing 4 kg. of crushed ice. The insoluble trinitrobenzoic acid is filtered off, and carefully washed with cold water until free from chromium salts. On drying it weighs 320–340 g.

The product is now mixed with 2 l. of distilled water at 35° in a 5-l. flask provided with a stirrer, and 15 per cent sodium hydroxide solution is dropped in with continuous stirring until a *faint* red color is just produced. Should this disappear, it is restored by the addition of a few drops more. When it has persisted for five minutes, the color is discharged by the addition of a few drops of acetic acid, and the insoluble unattacked trinitrotoluene filtered off and washed with a little water. The trinitrobenzoic acid is precipitated from the filtrate by the

addition of a slight excess of 50 per cent sulfuric acid. The solution is chilled, and the acid filtered and washed free from salts with ice water. When dried in air it weighs 230–280 g. (57 to 69 per cent of the theoretical amount).

## 2. Notes

The mother liquors and washings lose carbon dioxide on boiling, and the insoluble trinitrobenzene separates (see preparation XXIV); after filtering, washing, and drying, it weighs 15–20 g. (4 to 6 per cent of the theoretical amount).

It is essential that the stirring should be most efficient, so that when the mixture becomes thick the dichromate will be evenly distributed throughout the liquid, as rapidly as it is added. If the stirring is not efficient, local reactions of extreme violence (in certain cases leading to conflagration) will occur. An iron stirrer may be employed in the oxidation reaction, but not in the purification.

Technical sodium dichromate generally contains a certain amount of chlorides, and the chlorine liberated from these tends to cause a troublesome foam towards the end of the reaction. Only a very efficient stirrer, which draws down the surface of the liquid, is able to combat this difficulty. The amount of solid sodium dichromate given is for the dry crystalline compound containing two molecules of water of crystallization.

Great care should be taken in dissolving the crude acid in the alkali. If an excess of alkali persists for any length of time, a permanent color is produced which will discolor the final product. The acid is fairly soluble in cold water and should be washed with care.

## 3. Other Methods of Preparation

2, 4, 6-Trinitrobenzoic acid has been prepared by heating trinitrotoluene with fuming acid in a sealed tube to 100°, for two weeks,[1] the oxidation being only partial. It can also be prepared by heating trinitrotoluene under a reflux condenser, with a mixture of 5 parts of concentrated nitric acid and 10

[1] Ber. 8, 223 (1870).

parts of concentrated sulfuric acid;[1] this method is, however, unsuitable in the laboratory owing to the difficulty of devising suitable apparatus. Another method is to dissolve trinitrotoluene in nitric acid, and, to this solution (at 95°), to add potassium chlorate at such a rate that the temperature does not fall;[2] this method has been found to be difficult to control on a laboratory scale.

The method described above is a modification of a patented process,[3] in which trinitrotoluene suspended in sulfuric acid is treated with chromic anhydride.

[1] D. R. P. 77,559; Frdl. 4, 34 (1894).
[2] D. R. P. 226,225; Frdl. 10, 167 (1910).
[3] D. R. P. 127,325; Frdl. 6, 148 (1901).

# INDEX

# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS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# PREFACE TO VOLUME III

THE aims underlying the publication of this series have been made clear in the introductions in the first and second volumes. The program therein outlined has been adhered to, and efforts have been made to obtain and include as many contributions as possible from chemists other than the members of the Editorial Board. Thus out of the twenty-five preparations in Volume II, nine were provided by eight contributors; while in the present volume, thirteen contributors have supplied seventeen preparations out of a total of thirty. It is hoped that the number of contributors will continue to increase in subsequent volumes; and organic chemists not only in this country but abroad, are cordially invited to contribute work which they regard as suitable.

The Index in this volume refers to subjects not only in Vol. III but in Vols. I and II as well. It is planned to continue this collective Index in subsequent volumes.

The editors desire to express their sincere appreciation of the criticisms and corrections which have been extended, and their hope that this form of cooperation will be freely offered in the future as in the past. Their intention is to take advantage of all suggestions in the preparation of new editions.

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## I

## ACETAL

$$CH_3 \cdot CHO + 2C_2H_5OH \rightarrow CH_3 \cdot CH(OC_2H_5)_2 + H_2O$$

Prepared by Homer Adkins and B. H. Nissen.
Checked by H. T. Clarke and J. H. Bishop.

### 1. Procedure

In a 1-gallon bottle are placed 1050 g. of 95 per cent ethyl alcohol and 200 g. of granulated anhydrous calcium chloride (Note 1). The mixture is cooled to 8° or below by immersion in ice water, and 500 g. of freshly distilled acetaldehyde (B. P. 20–22°) is slowly added down the sides of the bottle so that it forms a layer on the alcoholic calcium chloride. The bottle is then tightly closed with a cork stopper and shaken vigorously for a few minutes (Note 2). It is then allowed to stand at room temperature with intermittent shaking for one to two days. The mixture divides into two layers after one to two hours; after the first twenty-four hours no appreciable change in volume of the two layers takes place.

The upper layer, which weighs 1280–1285 g., is separated and washed with 1000 cc. of water in three equal portions. The weight has now fallen to 990–995 g. The oil is dried by standing over 25 g. of anhydrous potassium carbonate and is then fractionally distilled with the use of an efficient column at least 90 cm. long (Note 3), and the fraction which boils at 101–103.5° collected as pure acetal. In this way 700–720 g. can be obtained by one or

two fractionations. The yield can further be increased by washing the low-boiling fractions and residue with small quantities of water, drying, and again fractionally distilling, so that a total of 790–815 g. is obtained (61–64 per cent of the theoretical amount).

## 2. Notes

1. It is essential that the calcium chloride should be anhydrous; if it contains water of crystallization, stratification may be long delayed and the yield be much decreased. On the other hand, no great advantage is observed by substituting absolute alcohol for the 95 per cent material.

2. On mixing the acetaldehyde and the alcoholic calcium chloride solution, a considerable rise in temperature takes place; for this reason it is necessary to chill the reagents and to close the stopper before mixing intimately; otherwise losses might occur by volatilization.

3. A fractionating column containing a condensing unit at the head [1] has been found satisfactory.

## 3. Other Methods of Preparation

Acetal has generally been prepared by the action of aldehyde upon alcohol in the presence of small quantities of mineral acid; [2] a patent has recently appeared [3] in which the formation of a 90 per cent yield of acetal by the action of certain metallic salts is claimed, but it has been found impossible to duplicate this result,[4] while the presence of mineral acid has been shown to act adversely on the yield.

[1] Ind. Eng. Chem. **15**, 349 (1923).
[2] Ann. **126**, 62 (1862); Ber. **30**, 3053 (1897).
[3] Brit. Pat. 101, 428 (1916); U. S. Pat. 1,312,186 (1919); C. A. **11**, 86 (1917).
[4] J. Am. Chem. Soc. **44**, 2749 (1922).

II

## ACETAMIDE

$$CH_3 \cdot CO_2NH_4 \rightarrow CH_3 \cdot CONH_2 + H_2O$$

Prepared by G. H. Coleman and A. M. Alvarado.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure

In a 5-l. flask is placed 3 kg. of glacial acetic acid and to this is added a weight of ammonium carbonate corresponding to 400 g. of ammonia (Note 1). The flask is fitted with a one-hole stopper holding an efficient fractionating column 90 cm. long with condenser and receiver. An air condenser 150–200 cm. long may be employed. The mixture in the flask is heated to gentle boiling and the flame so regulated that the rate of distillation does not exceed 180 cc. per hour. The distillation is continued in this way for eight to ten hours, until the temperature at the head of the column reaches 110°. The distillate, which is a mixture of water and acetic acid, amounts to 1400–1500 cc. The receiver is changed, the flame under the flask is gradually increased, and the distillation is continued at about the same rate until the temperature at the head of the column rises to 140°. The distillate, which amounts to 500-700 cc., is largely acetic acid and may be used in the next run.

The contents of the flask are transferred to a 2-l. flask for fractional distillation (as described in Vol. I, p. 40), having a column 40–50 cm. long, and distilled under atmospheric pressure, using an air condenser. The fraction boiling below 210°, amounting to 250–300 cc., is collected separately. The material remaining in the flask is nearly pure acetamide and may all be distilled, 1150–1200 g. passing over at 210–216°. By redistilling the fraction boiling below 210°, the yield may be

increased to 1200–1250 g. (87–90 per cent of the theoretical amount). The acetamide thus obtained is pure enough for most purposes, but if a purer product is desired it may be recrystallized from a mixture of benzene and ethyl acetate; 1-l. of benzene and 300 cc. of ethyl acetate are used for 1 kg. of acetamide. Colorless needles melting at 81° are thus obtained (Note 2). The solvent and the acetamide it contains may be recovered by distillation.

## 2. Notes

1. Ammonium carbonate of commerce is often extremely impure, and care must be taken to obtain a representative sample for the determination of the ammonia content by titration with standard acid. The ammonium carbonate used in this preparation contained 27.2 per cent of ammonia, and 1470 g. was used in each run.

2. As acetamide is somewhat hygroscopic, it cannot be exposed to the air unless precautions are taken to have the air dry.

## 3. Other Methods of Preparation

Acetamide has been prepared by a variety of methods, of which the more important are the following: by the rapid distillation of ammonium acetate;[1] by heating ammonium acetate in a sealed tube and distilling the product;[2] by treating acetic anhydride with ammonia;[3] by heating a mixture of ammonium chloride and sodium acetate to 240°;[4] by the action of cold aqueous ammonia on ethyl acetate;[5] by boiling a mixture of glacial acetic acid and ammonium thiocyanate for four days;[6] by saturating glacial acetic acid with dry ammonia and boiling;[7] by distillation of ammonium acetate through a reflux condenser

[1] Ann. **105**, 277 (1858).
[2] Ber. **15**, 977 (1882).
[3] Ann. chim. phys. (3) **37**, 327 (1853).
[4] J. Am. Chem. Soc. **24**, 762 (1902).
[5] Am. J. Sci. (4) **24**, 429 (1907).
[6] J. prakt. Chem. (2) **27**, 514 (1883).
[7] J. Am. Chem. Soc. **39**, 933 (1917).

filled first with glacial acetic acid and then with aniline until the temperature of the mixture reaches 220°.[8]

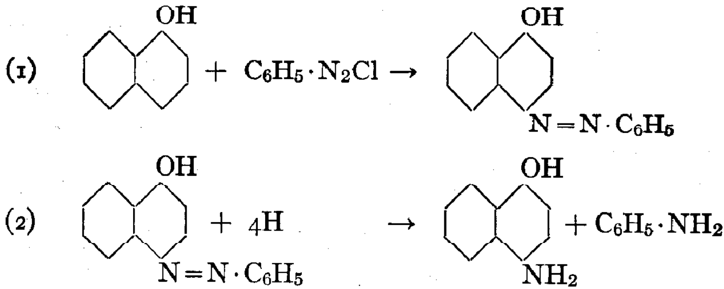
The foregoing process is based on the method of W. A. Noyes and W. F. Goebel,[9] in which equimolecular proportions of ammonium acetate and acetic acid are heated together, the acetic acid having been shown to accelerate both the dehydration of ammonium acetate and the hydrolysis of acetamide.

[8] J. Pharm. Chimie (6) **23**, 230 (Chem. Zentr. 1906 i, 1098).

[9] J. Am. Chem. Soc. **44**, 2286 (1922).

III

## 1,4-AMINONAPHTHOL HYDROCHLORIDE



Prepared by J. B. Conant, R. E. Lutz, and B. B. Corson.
Checked by H. T. Clarke and J. H. Bishop.

### 1. Procedure

In a 6-l. wide-mouth bottle, fitted with a mechanical stirrer and a separatory funnel, are placed 200 g. of α-naphthol melting at 91° or higher (Note 1) and 910 cc. of 10 per cent sodium hydroxide solution. The mixture is stirred for ten minutes, at the end of which time it has become a homogeneous solution.

While the naphthol is dissolving, a solution of benzenediazonium chloride is prepared. In a 3-l. wide-mouth bottle are placed 128 g. of aniline and 1.5 kg. of cracked ice, and on to this mixture while it is stirred (by hand) is poured 410 cc. of concentrated hydrochloric acid (32 per cent; sp. gr. 1.16). Some crystals of aniline hydrochloride separate at this point. A solution of 100 g. of sodium nitrite in 200 cc. of water is now run in slowly from a 500-cc. separatory funnel. The tip of the stem of the separatory funnel should dip well below the surface of the liquid. The mixture is stirred (by hand if desired) and a drop is tested from time to time with starch iodide paper. This is

best done by diluting the test-drop on a watch glass with about 1 cc. of water and then placing a drop of this solution on the starch iodide paper. The sodium nitrite solution is added until there is a test for nitrous acid which is permanent for five minutes. The diazotization is then complete; all but 2–5 per cent of the nitrite is required.

To the alkaline solution of α-naphthol is now added 1 kg. of cracked ice, the stirrer is started and the diazonium solution run in through a separatory funnel, the stem of which dips below the surface of the solution. The stirring must be uniform and efficient during the addition (Note 3). The addition of the diazonium solution should take ten minutes. Ice is added if necessary to keep the solution below 10°. The mixture is stirred for half an hour after the addition of the diazonium solution and then allowed to stand for three hours at 7–10° (Note 4), and finally filtered on a Buchner funnel, washed with a liter of water and sucked as dry as possible.

The moist benzeneazo-α-naphthol is next transferred to a 5-l. wide-mouth bottle or a 2-gal. crock equipped with a mechanical stirrer and containing 3 l. of 10 per cent sodium hydroxide solution. The mixture is stirred for ten minutes to insure solution of the dye, and then filtered. The insoluble solid is stirred up with 500 cc. of 10 per cent sodium hydroxide, filtered again and washed with water. *The solid, which weighs 10–90 g.*, consists mainly of the 2,4-disazo derivative (m. p. 197–198°), together with any benzeneazo-β-naphthol that may be present.

To the deep-red solution is added 550 g. of sodium hydrosulfite (of at least 80 per cent purity); the mixture is stirred for five minutes and then for five 30-second periods during half an hour (Note 5). The solution slowly loses its red color (a thin layer of aniline collects on the surface), and the temperature rises from 25° to 50°. At the end of half an hour the solution should no longer be red; it is then rapidly cooled to 20° in a freezing bath and by the addition of about 500 g. of ice.

To the solution is now added, with stirring, 625 cc. of concentrated (32 per cent; sp. gr. 1.16) hydrochloric acid (Note 6) or its equivalent of acid of approximately the same strength.

A cream-colored precipitate of the aminophenol forms. It is rapidly filtered off on a Buchner funnel (Note 7) and washed with one portion (200 cc.) of water about half saturated with sulfur dioxide. The precipitate soon darkens on exposure to air and is therefore rapidly transferred to a 2-gal. crock containing 2 l. of water and 340 cc. of concentrated hydrochloric acid. The soft lumps are broken up with a cork stopper set on the end of a stirring rod. Steam is passed into the mixture for 45 minutes, and during the last 30 minutes the mixture is stirred mechanically. At the end of this time the amine will have passed completely into solution. An insoluble impurity weighing 25–30 g. is removed by filtering with suction. The filtrate is cooled to 25° and if it is not clear is filtered again. To the clear solution at 25° is added 1200 cc. of concentrated hydrochloric acid with stirring, when a light gray precipitate of the aminophenol hydrochloride immediately forms. The solution is allowed to stand for two to three hours and is then filtered with suction. The hydrochloride is sucked as free from mother liquor as possible, washed with a little hydrochloric acid (1 vol. acid to 1 vol. of water), and dried on a porous plate. The liquors are concentrated to small volume under reduced pressure, and a second crop is thus obtained. The product is of a light purplish tint (Note 8) and weighs 175–200 g. (65–74 per cent of the theoretical amount, based on the quantity of α-naphthol employed).

## 2. Notes

1. Technical α-naphthol varies widely in purity, but material melting at 91° or above is substantially free of β-naphthol; unsatisfactory results will be obtained with material of an inferior grade, but when not more than 2 per cent of β-naphthol is present yields of 70 per cent should readily be obtained.

2. During the diazotization of the aniline the temperature must be kept at 0–5°. The amount of ice given above is usually enough for this, but if not, more must be added.

3. The stirring must be very uniform and vigorous during the addition of the benzenediazonium chloride solution to the

α-naphthol; otherwise the precipitate collects in gummy balls. If properly carried out, the operation produces a fine red precipitate which filters easily and is not at all gummy.

4. The temperature at which the coupling takes place and the mixture is allowed to stand has a great influence on the amount of disazo compound formed, as much as 120 g. being produced if no external cooling is provided.

5. The reduction with hydrosulfite may be carried out in an atmosphere of illuminating gas or hydrogen sulfide. The first precipitate of the free aminophenol is a little lighter in color when prepared in an inert atmosphere but the final aminonaphthol hydrochloride has the usual light purple color.

6. If too much hydrochloric acid is added in the precipitation of the free aminophenol, some will, of course, redissolve. The amount given above will give satisfactory results if the indicated quantities are adhered to.

7. The completeness of the precipitation should be tested by adding a little acid to one portion of the filtrate and a little sodium carbonate solution to another; no further precipitate should be produced in either case.

8. The aminophenol hydrochloride can be further purified by dissolving in hot water, cooling, and adding concentrated hydrochloric acid. It crystallizes in beautiful crystals, but the light violet color is very difficult to remove.

### 3. Other Methods of Preparation

1.4-Aminonaphthol has been prepared by the reduction of 1.4-nitronaphthol by tin and hydrochloric acid; [1] by the reduction with sodium amalgam of 1,4-aminonaphthol-3,8-disulfonic acid [2] or 1,4-aminonaphthol-5-sulfonic acid; [3] by the action of phenylhydrazine on 1,4-nitrosonaphthol.[4] The more usual preparative method has been to start with α-Naphthol Orange (Orange I) and reduce it with stannous chloride.[5]

[1] Ann. **183**, 247 (1876).
[2] Ber. **28**, 1536 (1895).
[3] Ann. **393**, 211 (1912).
[4] Gazz. Chim. Ital. (2) **25**, 393 (1895).
[5] Ber. **25**, 423 (1892); J. prakt. Chem. (2) **62**, 31 (1900); Ann. **211**, 61 (1882).

IV

# *p*-AMINOPHENYLACETIC ACID

$$NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H + 3(NH_4)_2S + 3H_2O \rightarrow$$
$$NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CO_2NH_4 + 3S + 5NH_4OH$$

$$NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CO_2NH_4 + CH_3 \cdot CO_2H \rightarrow$$
$$NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H + CH_3 \cdot CO_2NH_4$$

Prepared by G. Ross Robertson.
Checked by H. T. Clarke and J. H. Bishop.

## 1. Procedure

A 1500-cc. flask is fitted with a two-hole rubber stopper carrying a glass tube which ends below the middle of the flask. The second hole is fitted with a common glass stopcock (Note 1). To the flask is added 500 cc. of 6-N ammonium hydroxide (sp. gr. about 0.95), and 100 g. of *p*-nitrophenylacetic acid (Vol. II, p. 59) is now slowly introduced, with shaking. The flask is then placed in an ice bath, and the mixture saturated with hydrogen sulfide, the temperature being held below 50°.

The stopper is now removed from the reaction flask, and the solution (of ammonium *p*-aminophenylacetate) gently boiled under the hood until nearly all the excess hydrogen sulfide and ammonia have escaped. The solution changes from a dark orange-red to a pale yellow. The deposited sulfur is filtered off by suction, and 40 cc. of glacial acetic acid rapidly stirred into the hot filtrate. The *p*-aminophenylacetic acid which crystallizes out weighs 69–70 g., but it is contaminated with a small amount of free sulfur. On evaporating the mother liquor to a small volume, about 5 g. more can be obtained. The crude material is recrystallized from 4 l. of distilled water, 69–70 g. (83–84 per cent of the theoretical amount) of a product which melts at 199–200° being thus obtained.

## 2. Notes

1. The use of a stopcock in the reaction flask during the saturation with hydrogen permits the occasional expulsion of hydrogen gas, which would otherwise accumulate. Apparently, commercial ferrous sulfide contains free iron as an impurity.

2. The procedure avoids the troubles of filtration incidental to the method of reduction with ferrous sulfate and ammonia, and the yield is better. Inasmuch as the only by-product is the very soluble ammonium acetate, a large yield can be secured by close evaporation.

## 3. Other Methods of Preparation

*p*-Aminophenylacetic acid has been made by the hydrolysis of *p*-aminobenzyl cyanide[1] with concentrated hydrochloric acid; by the reduction of *p*-nitrophenylacetic acid with tin and hydrochloric acid,[2] or with ferrous sulfate and ammonia.[3]

[1] Ber. **17**, 237 (1884); **15**, 835 (1882).
[2] Ber. **2**, 209 (1869); J. Chem. Soc. **37**, 92 (1880).
[3] J. Am. Chem. Soc. **39**, 1437 (1917); **43**, 180 (1921).

# V

## ARSANILIC ACID

$$C_6H_5 \cdot NH_2 + H_3AsO_4 \rightarrow NH_2 \cdot C_6H_4 \cdot AsO_3H_2 + H_2O$$

Prepared by W. LEE LEWIS and H. C. CHEETHAM.
Checked by OLIVER KAMM and A. O. MATTHEWS.

### 1. Procedure

To 1035 g. of syrupy arsenic acid (80–85 per cent, sp. gr. 2.00/20°; Note 1) in a 12-inch evaporating dish, is added 828 g. (800 cc.) of aniline (Note 2) in 100-cc. portions; meanwhile, the lumps of aniline arsenate which are formed are broken up by rapid stirring with a porcelain spatula. When all the aniline has been added, the powdered solid is transferred to a 3-l. round-bottom flask equipped with a mechanical stirrer, a thermometer reaching to the lower part of the vessel, and a condenser arranged for downward distillation (Note 3); an additional 800 cc. of aniline is added and the flask slowly heated in an oil bath. The bath may be kept at a temperature not exceeding 170–175° as long as there is any considerable amount of unmelted material in the flask. When the contents of the flask have become liquid the temperature of the bath is dropped and the mixture held at 155–160° (inside temperature), with continual stirring, for at least four and a half hours. The mass will have assumed an intense violet color.

The reaction mixture is poured into 700 cc. of water and the flask is washed out with a portion of a previously prepared solution of 330 g. of sodium hydroxide in 1400 cc. of water, the washings being added to the reaction mixture. The remainder of the alkali is then added and the mixture agitated and cooled under the tap. At this point, two distinct layers are present, a lower pink-colored alkaline water layer, and an upper strongly

colored aniline layer. The water layer is, while warm, carefully separated from the purple-colored oil by means of a separatory funnel (heated to prevent the separation of sodium arsanilate) and after treatment with 15 g. of decolorizing carbon, is filtered through paper.

The arsanilic acid can be obtained from the aqueous alkaline solution either as the free acid or as the sodium salt. To obtain the free acid the solution is acidified with concentrated hydrochloric acid until the purple color of tetrabromophenolsulfonphthalein is changed to a faint yellow. Care should be taken, in the addition of the acid, not to overstep the end-point (Note 4). Crystallization is stimulated by scratching and the flask is allowed to stand over night to complete the precipitation. The crystals are filtered off and recrystallized once from water (about 2500 cc.) in order to obtain a white product. If the initial crystals obtained have an appreciable pink tinge, it is advisable to remove most of the color by digesting with a small volume of warm alcohol before crystallization from water is attempted (Note 5).

The yield of purified arsanilic acid obtained according to the above directions amounts to 250–300 g. (Note 6).

## 2. Notes

1. Arsenic acid obtained by oxidizing arsenious oxide with nitric acid is satisfactory; a syrupy acid of 80–85 per cent purity can be obtained on the market.

2. A good commercial grade of aniline, light in color and boiling with not more than 1° range, is suitable. It is not necessary to employ a freshly distilled product.

3. During the reaction a considerable amount of water escapes, together with aniline vapors, from the reaction vessel. The condenser is provided to condense and collect the distillate outside of the reaction flask, and thus minimize any danger from the aniline vapors. About 200 cc. of distillate will be obtained.

4. The precipitation of arsanilic acid from the reaction

mixture may cause difficulty if care is not taken to attain a definite hydrogen-ion concentration. The indicator consists of a 0.5 per cent solution of bromophenol blue. Filter paper dipped into this solution and dried forms a convenient test paper. That concentration which will cause a color change from purple to a faint yellow is considered the end-point. Congo Red may also be used as an indicator, but it is somewhat less sensitive.

5. A highly colored acid is occasionally obtained, and under such circumstances it may become essential to effect its purification by conversion into the sodium salt, followed by precipitation of the hot concentrated solution with alcohol, and regeneration of the acid. Colored impurities may also be eliminated by a process of fractional precipitation during the decomposition of the sodium salt, the impurities being separated with the first 25 g. fraction of the acid.

6. Additional amounts of arsanilic acid may be obtained from the various mother liquors. The products thus obtained are usually rather impure and hence are not considered in the yields quoted. On larger scale production it would be economical to recover this material as well as the excess aniline.

7. In preparing arsanilic acid upon a larger scale it was found that doubling the amount of aniline used and continuing the heating at 155° during twelve to sixteen hours resulted in a yield of 350–400 g. of recrystallized acid. For small scale work, when aniline is not recovered and when time is an important factor, the directions as presented seem preferable, particularly so since the arsanilic acid prepared during a short heating period is purified more readily.

### 3. Other Methods of Preparation

Arsanilic acid was prepared by Bechamp [1] by heating aniline arsenate to 190–200°. The product was originally described as the anilide of arsenic acid, but Ehrlich and Bertheim [2] showed its structure to be that of a true aryl arsenic acid.

[1] Compt. rend. 56, (1) 1172 (1863).

[2] Ber. 40, 3292 (1907).

The feasible methods of preparing arsanilic acid all depend upon the interaction between aniline and arsenic acid. Various temperatures ranging from 150 to 200° and various ratios of aniline to arsenic acid have been recommended.[3]

The main objection to most of the published methods is the fact that the authors leave it to be inferred that this is a smooth reaction. None of them points out the fact that an important side-reaction consists in the oxidizing action of arsenic acid upon aniline, with the production of a deeply purple-colored dye as well as much tarry material and some diaryl arsenic acid.

[3] Ber. **49**, 239 (1916); J. Am. Chem. Soc. **41**, 451 (1919); **42**, 828 (1920).

# VI

## BENZALACETONE

$$C_6H_5 \cdot CHO + CH_3 \cdot CO \cdot CH_3 \rightarrow C_6H_5 \cdot CH{=}CH \cdot CO \cdot CH_3 + H_2O$$

Prepared by N. L. DRAKE and P. ALLEN, JR.
Checked by C. S. MARVEL and A. W. SLOAN.

### 1. Procedure

IN a 2-l. bottle equipped with a mechanical stirrer are mixed 635 g. (800 cc.) of U. S. P. acetone (Note 2), 420 g. (400 cc.) of freshly distilled benzaldehyde boiling at 178–180° (shaken with dilute sodium carbonate just before distillation), and 400 cc. of water. To this mixture, 100 cc. of 10 per cent aqueous sodium hydroxide is slowly added from a dropping funnel (Note 3), while the solution is stirred and cooled by a water bath. The rate of addition of the alkali is so regulated that the temperature remains between 25 and 31°. This requires thirty to sixty minutes. The mixture is now stirred for two and a quarter hours at room temperature (Note 4). At the end of this time dilute hydrochloric acid is added until the mixture is acid to litmus. The two layers which form are separated in a separatory funnel. The lower aqueous layer is extracted with 100 cc. of benzene, and the benzene solution added to the yellow oil which formed the upper layer in the first separation. This benzene solution is shaken with 100 cc. of water and separated. The benzene is then removed by distilling from a steam bath, and the residue distilled under reduced pressure (Note 5), any water which condenses with the forerun being separated (Note 6). A special distilling flask with a fractionating side-arm (Vol. I, p. 40) is best employed. The material which distils at 148–160°/25 mm., 133–143°/16 mm., or 120–130°/7 mm. weighs 430–470 g. (Note 1); it solidifies to a crystalline mass on stand-

ing, and is pure enough for all practical purposes. On redistillation there is obtained 375–450 g. (65–78 per cent of the theoretical amount) of material boiling at 137–142°/16 mm. or 123–128°/8 mm., which solidifies on standing to crystals which melt at 40–42°.

## 2. Notes

1. Benzalacetone acts as an irritant, and care should be taken that it be not allowed to come in contact with the skin.

2. A large excess of acetone is taken, so as to diminish the formation of dibenzalacetone.

3. If the sodium hydroxide is added too rapidly and without cooling, the mixture darkens and the yield is lowered. The rate of addition is best determined by watching the temperature of the reaction mixture.

4. Instead of stirring the mixture after the addition of the sodium hydroxide, the bottle may be securely stoppered and shaken on a shaking machine for the same length of time.

5. The lower the pressure used in the distillation the less decomposition occurs, and the less residue is left in the distilling flask. This residue contains some dibenzalacetone.

6. The first few cubic centimeters of the distillate have a greenish color, but the rest is light yellow. For this reason it is desirable to collect the first of the distillate separately, if a very light-colored product is desired.

7. On exposure to air benzalacetone gradually turns brown, especially if it is slightly impure. Pure material can be kept for months in an ordinary stoppered bottle without changing color.

## 3. Other Methods of Preparation

Benzalacetone has been obtained in small yield by dry distillation of a mixture of calcium acetate and calcium cinnamate;[1] by heating the sodium derivative of cinnamaldehyde with methyl iodide;[2] by heating cinnamaldehyde and methyl alcohol with zinc chloride;[2] by heating acetone and benzaldehyde with acetic

[1] Ber. 6, 254 (1873).
[2] Ber. 6, 257 (1873).

anhydride or zinc chloride.[3] It is also formed when styrene and acetyl chloride are condensed by means of stannic chloride and the product is treated with diethylaniline;[4] and when the vapors of cinnamic acid and acetic acid are passed together over ferric oxide at 470–490°.[5] The only practical method, however, consists in condensing benzaldehyde and acetone by means of dilute aqueous alkali.[6]

[3] Ber. **14**, 2461 (1881).
[4] Compt. rend. **168**, 1052 (1919).
[5] Bull. soc. chim. (4) **15**, 326 (1914).
[6] Ann. **223**, 139 (1884); **294**, 275 (note) (1897).

# VII

## BENZOIC ANHYDRIDE

$$C_6H_5 \cdot CO_2H + (CH_3 \cdot CO)_2O \rightarrow C_6H_5CO \cdot O \cdot CO \cdot CH_3 + CH_3 \cdot CO_2H$$

$$C_6H_5 \cdot CO_2H + C_6H_5 \cdot CO \cdot O \cdot CO \cdot CH_3 \rightarrow (C_6H_5 \cdot CO)_2O + CH_3 \cdot CO_2H$$

Prepared by H. T. CLARKE and E. J. RAHRS.
Checked by ROGER ADAMS and P. K. PORTER.

### 1. Procedure

IN a 5-l. flask, provided with a two-hole stopper fitted with a 90-cm. fractionating column[1] and a dropping funnel, are placed 1500 g. of benzoic acid, 1500 g. of acetic anhydride, and 1 cc. of syrupy phosphoric acid. The mixture is very slowly distilled, at such a rate that the temperature of the vapor at the head of the column does not exceed 120° (Note 1). When 250 cc. of distillate has been collected, 250 g. of acetic anhydride is added, and distillation is continued. This process is again repeated, so that in all 2000 g. of acetic anhydride has been taken. Fractionation is then continued, fractions which distil respectively below 120°, at 120–130°, and at 130–140° being collected. Heating is continued until the temperature of the reaction mixture in the flask reaches 270°.

The residue is fractionally distilled under reduced pressure, resulting in the collection of fractions which boil respectively below 165°, at 165–210°, and at 210–220°, all under 19–20 mm. pressure (Note 2). The lower fractions are mixed with the fraction which boils at 120–130°, and distilled as before after the addition of one drop of phosphoric acid, when a further quantity

[1] Ind. Eng. Chem. 15, 349 (1923).

of material boiling at 210–222°/20 mm. is obtained. This fraction, amounting to 1100–1200 g., consists of crude benzoic anhydride. The lower-boiling fractions may be redistilled until they become too small to justify further work.

The fraction which boils at 120–130° under atmospheric pressure is redistilled, yielding further quantities of acetic acid (below 120°) and acetic anhydride (130–140°).

The crude benzoic anhydride (which is apt to supercool without crystallizing) contains a small proportion of an oily impurity which causes the product to turn yellow on standing; it is recrystallized by dissolving in benzene (50 cc. for each 100 g.) then adding just enough petroleum ether to cause a cloudiness (about 100 cc. is required) and chilling, when the pure anhydride separates in perfectly colorless and odorless crystals melting at 43°. The first crop amounts to about 50 per cent of the crude material taken; the mother liquors are freed of solvent by distillation on the water bath, and the residue distilled under reduced pressure, when a further quantity of pure material can be obtained by recrystallizing the distillate boiling at 210–220°/19 mm. If this process is repeated until the mother liquor becomes too small in amount to redistil satisfactorily, the yield of pure benzoic anhydride melting at 43° amounts to 1000–1030 g. (72–74 per cent of the theoretical amount). It is generally more convenient to distil the mother liquors only once or possibly twice, under which conditions a somewhat lower yield is obtained. The remaining mother liquors may then be mixed with a subsequent preparation.

## 2. Notes

1. As it is probable that the equilibria between the two acids and the three anhydrides are established in reactions of relatively low velocity, the distillation must be carried on very slowly, in spite of the catalytic action of the phosphoric acid. The intermediate fractions contain the mixed anhydride, detectable by its odor, which resembles that of acetophenone.

2. Owing to the high boiling-point of the end-product, the second stage must be conducted under reduced pressure. The

temperatures indicated depend, of course, upon the pressure under which the distillation is carried out, and allowances will have to be made for pressures differing materially from 20 mm.

3. Although the yield above quoted is by no means quantitative, the only reason why it should not be made nearly so by continual redistillation of the various fractions in presence of the catalyst lies in the length of time required for the process. This, however, could be avoided if a large number of runs were to be made, when the intermediate fractions could be worked over repeatedly with each subsequent batch, until practically nothing but acetic acid and benzoic anhydride remained.

### 3. Other Methods of Preparation

Benzoic anhydride has been prepared in rather a poor yield by the action of benzoyl chloride on sodium benzoate,[2] barium oxide at 150°,[3] benzoic acid at 160–200°,[4] sodium nitrite,[5] lead nitrate,[6] or anhydrous oxalic acid;[7] also by treating sodium benzoate with phosphorus pentachloride[8] or sulfur chloride.[9] More important methods consist in treating benzotrichloride with sulfuric acid,[10] and in the action of sodium carbonate upon benzoyl chloride in presence of pyridine.[11]

By heating benzoic acid with acetic anhydride in a closed vessel at 220°, a poor yield of benzoic anhydride is obtained;[12] a 50 per cent yield is obtained by boiling benzoic acid with three times its weight of acetic anhydride and distilling the mixture.[13]

Numerous patents have appeared in which benzoic anhydride has been prepared: by the action of benzenesulfochloride upon

[2] Ann. **87**, 73 (1853).
[3] Ann. **128**, 127 (1863).
[4] Ann. **226**, 5 (1884).
[5] Gazz. Chim. Ital. **20**, 655 (1890).
[6] Ber. **17**, 1282 (1884).
[7] Ann. **226**, 15 (1884).
[8] Jahresb. **1854**, 409.
[9] Jahresb. **1856**, 464.
[10] D. R. P. 6,685; Frdl. **1**, 24 (1877–87).
[11] Gazz. Chim. Ital. **22**, 215 (1892); J. prakt. Chem. (2) **50**, 479 (1894).
[12] Ann. **226**, 12 (1884).
[13] Ber. **34**, 184 (1901).

sodium benzoate;[14] by the action of chlorosulfonic acid upon potassium benzoate;[15] by the action of silicon tetrachloride upon sodium benzoate;[16] by the action of sulfuryl chloride upon a mixture of calcium benzoate and sodium sulfate or sodium chloride;[17] by the action of sulfuryl chloride upon a mixture of 2 mols. of sodium benzoate and 1 mol. of calcium benzoate;[18] by the action of sulfur dioxide and chlorine upon sodium benzoate;[19] by the action of sulfuric anhydride upon a mixture of benzoic acid and sodium benzoate;[20] by the action of a mixture of sulfuric anhydride and carbon tetrachloride on sodium benzoate.[21]

It is probable that some of these patented processes would be more suitable for the commercial preparation of benzoic anhydride, but the method given in the procedure is satisfactory for the laboratory.

[14] D. R. P. 123,052; Frdl. **6**, 35 (1900–02).
[15] D. R. P. 146,690; Frdl. **7**, 28 (1902–04).
[16] D. R. P. 171,146; Frdl. **8**, 69 (1905–07).
[17] D. R. P. 171,787; Frdl. **8**, 68 (1905–07).
[18] D. R. P. 161,882; Frdl. **8**, 66 (1905–07).
[19] D. R. P. 210,805; Frdl. **9**, 68 (1907–10).
[20] D. R. P. 286,872; Frdl. **12**, 77 (1914–16).
[21] D. R. P. 290,702; Frdl. **12**, 79 (1914–16).

# VIII

## β-BROMOPROPIONIC ACID

$$CH_2OH \cdot CH_2 \cdot CN + 2HBr + H_2O \rightarrow CH_2Br \cdot CH_2 \cdot CO_2H + NH_4Br$$

Prepared by E. C. KENDALL and B. McKENZIE.
Checked by H. T. CLARKE and M. R. BRETHEN.

### 1. Procedure

To 2000 cc. of 40 per cent hydrobromic acid (Note 1) in a 3-l. flask is added 317 g. of ethylene cyanohydrin (p. 57), and the mixture is boiled for two hours under a reflux condenser. The condenser is then arranged for downward distillation and a thermometer immersed in the reaction mixture; dilute hydrobromic acid is distilled off until the temperature in the flask reaches 121°, whereupon the receiver is changed and a fraction consisting of stronger hydrobromic acid is collected over the range 121–129°. When the temperature of the mixture reaches 129°, very little hydrobromic acid remains, and on cooling, the mass sets to an almost colorless solid. This is now dissolved in 2000 cc. of carbon tetrachloride (Note 2), and the ammonium bromide is filtered off and washed with 500 cc. more of the solvent; a thin aqueous layer is separated and 1500 cc. of the carbon tetrachloride distilled from the filtrate. On cooling, about 470 g. of β-bromopropionic acid crystallizes from the residue; on filtering off and drying, this melts at 62.5–63.5°. On further concentration, the mother liquor yields a second crop of β-bromopropionic acid, amounting to 60–70 g.

The aqueous layer separated from the main carbon tetrachloride solution is shaken out with 100 cc. of carbon tetrachloride, and thus yields about 10 g. of pure acid; when the dilute and the concentrated hydrobromic acid fractions are extracted in the same way, about 5 g. and 15 g. respectively of

β-bromopropionic acid are obtained. The total yield is 560–570 g. (82–83 per cent of the theoretical amount).

## 2. Notes

1. The 2 l. (2750 g.) of 40 per cent hydrobromic acid may advantageously be replaced by a corresponding quantity (1550 cc.) of constant-boiling 48 per cent hydrobromic acid, should this be available.

2. In no case should benzene be used in place of carbon tetrachloride, as it has been found impossible to separate this solvent from β-bromopropionic acid, even on repeated fractionation with an efficient column.

## 3. Other Methods of Preparation

The chief methods for the preparation of β-bromopropionic acid are the action of hydrobromic acid on acrylic acid,[1] on hydracrylic acid,[2] and on ethylene cyanohydrin;[3] the oxidation of β-bromopropionaldehyde[4] and of trimethylene bromohydrin[5] with nitric acid.

[1] Ann. **163**, 96 (1872); **342**, 127 (1905).
[2] Ber. **18**, 227 (1885).
[3] J. Am. Chem. Soc. **39**, 1466 (1917).
[4] J. prakt. Chem. (2) **42**, 384 (1890); Bull. soc. chim. (3) **9**, 388 (1893).
[5] Ber. **54B**, 3117 (1921).

IX

## CATECHOL

### A. (*from Salicylaldehyde*)

$$C_6H_4(ONa) \cdot CHO + H_2O_2 \rightarrow C_6H_4(OH)_2 + HCO_2Na$$

Prepared by H. D. DAKIN.
Checked by H. T. CLARKE and E. R. TAYLOR.

### 1. Procedure

To a solution of 122 g. of pure salicylaldehyde (Note 1) in 1000 cc. of normal sodium hydroxide solution at room temperature, is added 1420 g. of 3 per cent hydrogen peroxide. The mixture darkens slightly in color and the temperature rises to 45–50°. The solution is allowed to stand for fifteen to twenty hours, whereupon a few drops of acetic acid are added in order to neutralize any excess alkali, and the solution evaporated to complete dryness on the water bath under reduced pressure.

The solid residue is finely crushed and warmed nearly to boiling with 500 cc. of toluene; the mixture is then poured on to the folded filter paper of an extraction apparatus (Vol. II, p. 49) and extracted with boiling toluene for five hours. The toluene is allowed to cool and is decanted from the catechol, which crystallizes out. The insoluble material is again ground up and extracted in the apparatus with the decanted toluene. The combined product, weighing 70–76 g., consists of light brown plates melting at 104°, and is thus pure enough for many purposes. A further 6–12 g. of catechol can be obtained on distilling off the bulk of the toluene from the mother liquor. In order to obtain an entirely pure product, the crude catechol should be distilled under reduced pressure, when it passes over entirely at 119–121°/10 mm. (or 113–115°/8 mm.), and the

distillate recrystallized from about five times its weight of toluene. In this way, colorless plates melting at 104–105° are obtained. Yield 76–80 g. (69–74 per cent of the theoretical amount).

## 2. Notes

1. A considerably lower yield is obtained (50 per cent or less) if technical salicylaldehyde (not purified through the bisulfite compound) be employed.

2. The above process is applicable to almost all hydroxyaldehydes in which the hydroxyl and carbonyl groups occupy ortho or para positions relatively to each other;[1] in the latter case derivatives of hydroquinone are produced. When the hydroxyl and carbonyl groups occupy the meta position with respect to each other, no reaction takes place, as is also the case with certain ortho and para compounds containing nitro groups and iodine atoms. *o*-Hydroxyacetophenone and *p*-hydroxyacetophenone are also capable of yielding catechol and hydroquinone respectively under the above conditions.

3. Catechol may also be produced from salicylaldehyde by the use of certain derivatives of hydrogen peroxide, such as persulfates or sodium peroxide, but the method is far less convenient.

### B. (*from Guaiacol*)

$$CH_3O \cdot C_6H_4 \cdot OH + HBr \rightarrow C_6H_4(OH)_2 + CH_3Br$$

Prepared by H. T. Clarke and E. R. Taylor.
Checked by C. S. Marvel and W. B. King.

## 1. Procedure

In a 5-l. flask fitted with a stirrer, a thermometer reaching to the bottom, a fractionating column about 40 cm. long (Note 2), and a return inlet tube, are placed 912 g. of crystalline guaiacol and 1500 g. of 48 per cent hydrobromic acid. This apparatus is connected with a condenser, an automatic separator, and an absorption vessel, as shown in the diagram (Note 1). The

[1] Am. Chem. J. 42, 477 (1909).

mixture is gently heated, with continual stirring, at such a rate that the vapor at the head of the column maintains a temperature of 85–95°. The mixture of water and guaiacol which condenses passes through the automatic separator (Note 3), the guaiacol being returned to the reaction vessel and the water collected in the tap funnel, from which it is removed from time

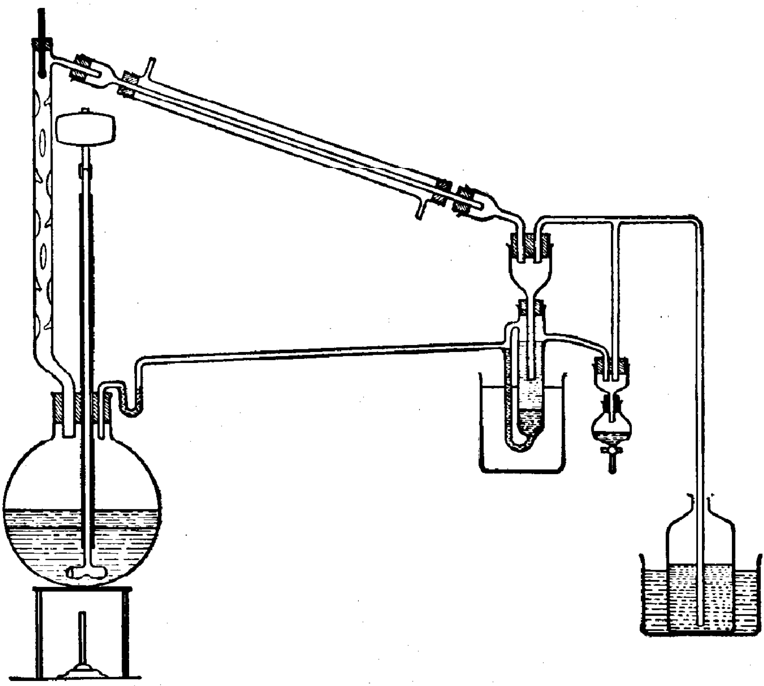


FIG. 1.

to time. The gaseous methyl bromide is collected in an ice-cooled bottle containing a weighed quantity (about 1600 g.) of methyl alcohol (Note 4).

After six to seven hours, the temperature at the head of the column begins to rise above 95° and finally reaches 98°, at which point practically no more guaiacol passes over with the distillate. This requires about one hour more, after which the heating is stopped (Note 5). The increase in weight of the absorption

bottle amounts to 400–500 g. (53–66 per cent of the theoretical amount of methyl bromide); the water collected weighs 550–560 g. (Note 6).

The residue in the flask, which has become pink in color, is extracted at 85–95° with three 1500-cc. portions of toluene, and the united extracts are distilled under reduced pressure on the steam bath until no more moisture passes over with the vapor. The solution (2–2.5 l.) is then allowed to cool, whereupon 385–390 g. of catechol separates in colorless plates melting at 104–105°. The mother liquor is further concentrated under reduced pressure and the residue finally distilled, pure catechol passing over at 124–125°/12 mm. The distillate, on recrystallization from a small quantity of toluene, yields 8–10 g. of pure material.

The aqueous residue from the three extractions with toluene yields, when the bulk of the water has been distilled off on the steam bath under reduced pressure, a further quantity of catechol by extraction with hot toluene, but the crystals so obtained are contaminated with a red impurity. It is therefore preferable to distil the entire residue, again collecting the fraction boiling at 124–125°/12 mm. and recrystallizing it from fresh toluene. In this way 295–305 g. of pure product is obtained. The forerun contains a little aqueous hydrobromic acid, which may be employed in a subsequent batch. The total yield of pure catechol is 690–705 g. (77–80 per cent of the theoretical amount).

## 2. Notes

1. In the diagram (Fig. 1) no indication is made of joints in the glass tubing. These are, however, applicable at almost any desired point; but care should be taken to arrange them so that the ends of the glass tube come into contact, since methyl bromide appears to pass readily through the walls of the india rubber tubing. It is necessary to make certain that the outlets from the automatic separator descend in an even incline and that the tubing itself is of sufficiently large diameter to prevent any siphoning effects.

2. Any column of standard form is suitable; to work satisfactorily, it is unnecessary for it to be more than 40 cm. in length.

3. It is noteworthy that the guaiacol which condenses is saturated with methyl bromide at the condensation temperature, so that it is necessary to prevent it from becoming warmer during its passage through the separator; otherwise the evolution of gas may hinder the ready formation of layers.

4. In order to secure satisfactory absorption of the methyl bromide, the methyl alcohol should be kept below 5° by ice-cooling.

5. Since the formation of the red by-product appears to depend upon the time during which the catechol is heated with hydrobromic acid, it is well to carry out the reaction as rapidly as possible; due care must be taken, however, that the temperature at the head of the column does not rise prematurely above 95°.

6. The water collected during the reaction contains practically no hydrobromic acid but is saturated with guaiacol and methyl bromide. Nevertheless, it scarcely pays to recover the dissolved compounds, for on distillation only 1-2 g. of wet guaiacol can be collected; while the value of the methyl bromide is in any case not very great.

7. The reaction appears to be applicable to many other cases where the constitution of the molecule permits of boiling with strong hydrobromic acid.

## 3. Other Methods of Preparation

The general reaction upon which the first of the above two methods is based is that described by Dakin in 1909;[2] the demethylation of guaiacol to catechol has been effected by heating with aluminum chloride[3] and with hydriodic acid.[4] Other important methods of preparation consist in treating ortho halogen-substituted phenols with alkalies under suitable

[2] Am. Chem. J. **42**, 477 (1909).

[3] Ber. **25**, 3532 (1892); D. R. P. 70,718, Frdl. **3**, 52 (1890–94).

[4] Ber. **8**, 153 (1875); J. Chem. Soc. **57**, 587 (1890).

conditions;[5] replacement of sulfonic groups[6] or amino groups[7] by hydroxyl; and oxidation of phenol[8] or benzene[9] by means of hydrogen peroxide. The majority of these, however, are unsuitable as laboratory methods.

[5] Ann. **120**, 315 (1861); Z. **1868**, 322; D. R. P. 84, 828, Frdl. **4,** 114 (1894–97); D. R. P. 249,939, Frdl. **10**, 1330 (1910–12); D. R. P. 269,544, Frdl. **11**, 190 (1912–14); Cf. Ber. **8**, 363 (1875).

[6] Z. **1867**, 643; D. R. P. 80,817, Frdl. **4**, 116 (1894–97); D. R. P. 81,209, Frdl. **4**, 117 (1894–97).

[7] Ber. **30**, 2568 (1897); D. R. P. 167,211, Frdl. **8**, 128 (1905–07).

[8] Bull soc. chim. (2) **43**, 157 (1885).

[9] Ber. **33**, 2017 (1900).

X

## *o*-CHLOROTOLUENE AND *p*-CHLOROTOLUENE

$$CH_3 \cdot C_6H_4 \cdot NH_2 + HNO_2 + HCl \rightarrow CH_3 \cdot C_6H_4 \cdot N_2Cl + 2H_2O$$
$$CH_3 \cdot C_6H_4 \cdot N_2Cl + CuCl \rightarrow CH_3 \cdot C_6H_4 \cdot Cl + N_2 + CuCl$$

Prepared by C. S. Marvel and S. M. McElvain.
Checked by Oliver Kamm.

### 1. Procedure

A. *Preparation of the cuprous chloride solution.* A solution of 1250 g. (5 mols.) of crystallized copper sulfate and 325 g. (5.6 mols.) of sodium chloride in 4 l. of hot water is prepared in a 12-l. flask. The flask is fitted with a mechanical stirrer, and an alkaline solution of sodium sulfite (265 g. of sodium bisulfite and 175 g. of sodium hydroxide in 2 l. of water) is added during a period of five to ten minutes. The mixture is allowed to cool to room temperature and washed by decantation. The cuprous chloride is obtained as a white powder, which, however, darkens on exposure to the air. The crude product is dissolved in 2 kg. of commercial 28 per cent hydrochloric acid (sp. gr. 1.14) and the solution is used in the following preparation.

B. *Preparation of chlorotoluene.* In a 10-l. stone jar fitted with a mechanical stirrer are placed 2 kg. of commercial 28 per cent hydrochloric acid (sp. gr. 1.14) and 428 g. (4 mols.) of *o*-toluidine. The mixture is cooled to 0° by adding cracked ice (about 1 kg. is required). The *o*-toluidine hydrochloride separates as a finely divided precipitate. The stirrer is started, and to the cold suspension is added a solution of 280 g. (4.05 mols.) of sodium nitrite in 800 cc. of water; the diazotization is carried out at 0–5° and requires about fifteen minutes. Cracked ice is added from time to time to keep the temperature within the proper limits. The volume of the final solution is 5–6 l.

While the diazotization is being carried out the cuprous chloride solution is cooled to 0°. The cold diazonium solution is now poured rapidly into the well-stirred cuprous chloride solution. The solution becomes very thick, owing to the separation of an addition product between the diazonium salt and the cuprous chloride. The cold mixture is allowed to warm up to room temperature, and stirring is continued for two and a half to three hours at this temperature (Note 3). When the temperature reaches about 15°, the solid addition compound begins to break down with the formation of nitrogen and *o*-chlorotoluene. After the specified time the solution is placed on a steam bath and heated to 60° to complete the decomposition of the addition product. The *o*-chlorotoluene forms a layer on top of the copper salt solution. The water solution is drawn off through a siphon until only 5–6 l. remains. The remaining material is steam-distilled from a 12-l. round-bottom flask (Note 4) until about 3.5–4 l. is collected in the distillate. The *o*-chlorotoluene layer is separated from the water, washed with cold concentrated sulfuric acid (Note 5), then with water, and is finally dried over calcium chloride. The product boiling at 155–158° weighs 375–400 g. (74–79 per cent of the theoretical amount).

*p*-Chlorotoluene is prepared in exactly the same way starting with *p*-toluidine. The yields are 70–79 per cent of the theoretical amount of a product which boils at 158–162° and melts at 4–7°.

## 2. Notes

1. The cuprous chloride solution prepared as described above is more satisfactory and cheaper than one prepared by reducing cupric chloride with copper turnings.

2. If less cuprous chloride is used the yield is lowered. It seems desirable to use 1 mol. of cuprous chloride (CuCl) to 1 mol. of diazonium salt. Increasing the amount of cuprous chloride beyond this point does not improve the yield.

3. The literature directions usually call for mixing the diazonium solution and the cuprous chloride solution at about 30–40°. This procedure gives a yield considerably lower than

that obtained by mixing the solutions cold and allowing to warm up gradually. If the mixture obtained by adding the diazonium solution to the cuprous chloride solution is heated at once, the yield falls to 55–65 per cent.

4. The steam distillation can be conveniently carried out in the apparatus used in the steam distillation of quinoline (Vol. II, p. 80).

5. The treatment with sulfuric acid is necessary to remove cresol and a trace of azo compound that usually colors the crude product and cannot be removed by distillation.

## 3. Other Methods of Preparation

*o*-Chlorotoluene has been obtained by the action of chlorine on toluene in the presence of various catalysts;[1] by the action of sulfuryl chloride on toluene in the presence of aluminum chloride;[2] by the chlorination of *p*-toluenesulfochloride followed by hydrolysis;[3] by the diazotization of *o*-toluidine followed by replacement of the diazonium salt group by chlorine.[4]

*p*-Chlorotoluene has been obtained by the action of chlorine on toluene in the presence of various catalysts;[5] by the action of sulfuryl chloride on toluene in the presence of aluminum chloride;[6] by the electrolytic reduction of *p*-chlorobenzaldehyde;[7] by the diazotization of *p*-toluidine followed by replacement of the diazonium salt group with chlorine.[8]

[1] Ber. **6**, 790 (1873); Ann. **237**, 152 (1887); Compt. rend. **135**, 1121 (1902).

[2] Rec. trav. chim. **30**, 387 (1911).

[3] D. R. P. 133,000; Chem. Zentr. **1902** (2), 313; D. R. P. 294,638; C. A. **11**, 2582 (1917).

[4] Ann. **247**, 367 (1888); **269**, 394 (1892); **272**, 145 (1893); Ber. **18**, 1939 (1885); **23**, 1221 (1890); **44**, 254 (1911); Z. physik. Chem. **4**, 71 (1889); Z. angew. Chem. **23**, 392 (1910).

[5] Ann. **139**, 334 (1866); **237**, 152 (1887); Ber. **6**, 790 (1873); **8**, 1402 (1875).

[6] Ber. **26**, 2941 (1893); Rec. trav. chim. **30**, 387 (1911).

[7] J. Chem. Soc. **99**, 1114 (1911).

[8] Ber. **6**, 794 (1873); **18**, 1939 (1885); **23**, 1221 (1890); **44**, 254 (1911); Z. angew. Chem. **23**, 392 (1910).

XI

# *p*-CRESOL

$$CH_3 \cdot C_6H_4 \cdot SO_3Na + KOH \rightarrow CH_3 \cdot C_6H_4 \cdot OH + KNaSO_3$$

Prepared by W. W. Hartman.
Checked by Roger Adams and A. W. Sloan.

## 1. Procedure

One kg. of technical sodium hydroxide and 400 g. of technical potassium hydroxide (Note 2) are melted together in a cast-iron flat-bottom kettle, 18 cm. in depth and 18 cm. in diameter. The fused mass is well stirred by means of a piece of iron pipe closed at one end, containing a thermometer; the hand is protected by an india rubber glove wrapped with a cloth. The temperature of the fused mass is allowed to fall to 230°, and 150 g. of technical sodium *p*-toluenesulfonate is stirred in. The temperature is now slowly raised while 450 g. more of sodium *p*-toluenesulfonate is added slowly, the additions being made whenever the melt becomes sufficiently thin to stir in the solid. When all has been added, the temperature should be about 270°; the addition requires about thirty minutes. The temperature is now raised to 300°, with occasional stirring. At this point there is a layer of heavy froth on the surface of the thin melt, and as the temperature rises this is stirred in, the whole melt becoming frothy and showing a tendency to foam over. On continuing to raise the temperature, the foaming suddenly disappears at about 330°; the melt becomes dark and evolution of hydrogen sets in. The mixture is now thin and of uniform consistency; it is poured at once into an iron tray and allowed to cool.

The solidified product is dissolved in 6–7 l. of water in a 12-l. flask, and a solution of concentrated (95 per cent) sulfuric

acid (about 880 cc.) in about 2 l. of water is added until the liquor has a distinct odor of sulfurous acid. The heat of neutralization is sufficient to cause the solution to boil; it is at once distilled in a current of steam (Note 3) until a sample of the distillate gives only a slight precipitate with bromine water. The distillate (about 6–7 l.) is saturated with salt and the oil separated. The watery solution may be again distilled with steam in order to recover the small amount of cresol in solution. The oil is at once distilled under reduced pressure, and the fraction which boils at 95–96°/15 mm. is collected. The forerun is freed of water and redistilled, yielding a further quantity. On *cooling, the product solidifies to a white, crystalline mass melting at* 31°. The yield is 200–230 g. (60–70 per cent of the theoretical amount).

## 2. Notes

1. Technical sodium *p*-toluenesulfonate is, as a rule, of about 95 per cent purity; it contains about 2 per cent of sodium chloride and some moisture. Attempts to prepare a *p*-cresol of higher melting point by fusion of recrystallized sodium *p*-toluenesulfonate (which should presumably contain no isomers) have failed; it has been found impossible to raise the melting point above 31.4°.

2. Fusion with sodium hydroxide alone yields no cresol, the fused sodium hydroxide appearing to have no solvent action on the sodium *p*-toluenesulfonate. On the other hand, potassium hydroxide works entirely satisfactorily, as do mixtures of sodium hydroxide and potassium hydroxide containing not less than 28 per cent of potassium hydroxide. In the above directions the minimum amount of potassium hydroxide is indicated.

3. Since distillation in a current of steam in a laboratory is apt to be a tedious process when only the regular form of Liebig condenser is employed, much time can be saved by the use of the apparatus described in Vol. II, p. 80.

## 3. Other Methods of Preparation

The only other important method by which *p*-cresol can be prepared is decomposition of diazotized *p*-toluidine;[1] the yield is not very good, however, and the quality of the product is almost always poor. The literature also contains methods for its formation from *p*-toluenesulfonic acid by fusion with potassium hydroxide.[2]

[1] Jahresb. **1866**, 458; Z. **1868**, 325.
[2] Ann. **144**, 122 (1867); **156**, 258 (1870); Z. **1869**, 618.

## XII

# 9,10-DIBROMOANTHRACENE

$$C_{14}H_{10}+2Br_2 \rightarrow C_{14}H_8Br_2+2HBr$$

Prepared by I. M. HEILBRON and J. S. HEATON.
Checked by H. T. CLARKE and T. F. MURRAY.

## 1. Procedure

To a suspension of 300 g. of anthracene of 80–85 per cent purity in 3 l. of carbon tetrachloride, in a 5-l. flask fitted with dropping funnel, stirrer, and reflux condenser, is added slowly 567 g. of bromine. The bromination takes place in the cold with separation of the sparingly soluble 9,10-dibromoanthracene; in order to prevent undissolved anthracene from becoming coated over, it is necessary to maintain vigorous stirring throughout the reaction. A tube from the top of the condenser conducts hydrogen bromide to cold water, in which it is absorbed. The addition of the bromine occupies about half an hour; the rate is so adjusted that a minimum of bromine is carried over with the hydrogen bromide.

When all the bromine has been added, the mixture is gently warmed on a steam bath with continual stirring, care being taken not to heat so rapidly as to cause undue loss of bromine by entrainment. Heating is continued until the mixture has boiled gently for an hour. The mixture is then allowed to cool for some hours, without stirring, and the crude dibromoanthracene is filtered off, washed with a little cold carbon tetrachloride, and dried. In this way 270–425 g. of a bright yellow product, which melts (Note 4) at 218–219° (corr.), is obtained. On concentrating the mother liquors, 15–150 g. more of crude material (m. p. about 216° corr.) can be obtained.

To prepare an absolutely pure product, the crude dibromo-

anthracene is extracted with carbon tetrachloride (Note 2) in an apparatus similar to that described in Vol. II, p. 49; the extraction is carried to the point at which crystals just begin to separate from the boiling solvent, and a fresh quantity of carbon tetrachloride is then taken. About eight extractions are necessary, 1 l. being used each time. The 9,10-dibromoanthracene so purified consists of brilliant yellow needles melting at 221–222° (corr.). A further quantity of pure product may be obtained by concentrating the mother liquor and recrystallizing the second crop so obtained. The recovered solvent may be employed for further extractions. The yield amounts to 400–420 g. (83–88 per cent of the theoretical quantity based on anthracene of 85 per cent purity).

## 2. Notes

1. The reaction may be carried out equally well with a larger proportion of solvent, but if less than the amount indicated be taken, difficulty may arise in stirring. Carbon bisulfide may be employed instead of carbon tetrachloride, but this solvent presents no essential advantages and it is necessary to use a larger volume for the same amount of anthracene.

2. The crude product may be recrystallized from toluene, in which it is somewhat more soluble than in carbon tetrachloride; the color of the product is, however, not quite so light, although the melting point is as high as if carbon tetrachloride were used. If desired, recrystallization may be effected from toluene without using the extraction apparatus, in which case about 10 l. of solvent in all will be required; for the filtration of the hot solution, a plug of glass wool, previously wetted with boiling xylene, may be employed, care being taken to warm the funnel adequately.

3. The bromination products of the impurities with which commercial anthracene is contaminated appear to be more soluble in carbon tetrachloride than in 9,10-dibromoanthracene; the yield can be slightly increased by fractional recrystallization of the products contained in the original mother liquor, but

under laboratory conditions the gain does not compensate for the time involved.

4. The observed melting-points of the various products are 5–6° lower than the corrected values.

5. The watery solution of hydrogen bromide, on fractional distillation, readily yields 48 per cent hydrobromic acid, boiling at 125–126°/760 mm. (cf. Vol. I, p. 2).

### 3. Other Methods of Preparation

The only preparative method to be found in the literature [1] consists in the bromination of anthracene in dilute carbon disulfide solution.

[1] Ann. Suppl. **7**, 275 (1870).

## XIII

# DIPHENYLACETIC ACID

$$(C_6H_5)_2C(OH) \cdot CO_2H + 2H \rightarrow (C_6H_5)_2CH \cdot CO_2H + H_2O$$

Prepared by C. S. Marvel, F. D. Hager and E. C. Caudle.
Checked by J. B. Conant and A. W. Sloan.

### 1. Procedure

In a 1-l. round-bottom flask are placed 250 cc. of glacial acetic acid, 15 g. of red phosphorus and 5 g. of iodine. The mixture is allowed to stand for fifteen to twenty minutes until the iodine has reacted, and then 5 cc. of water and 100 g. of benzilic acid are added. A reflux condenser is attached and the mixture is boiled continuously for at least two and a half hours. After the reaction is complete, the hot mixture is filtered with suction to remove the excess red phosphorus (Note 2). The hot filtrate is slowly poured into a cold, well-stirred, filtered solution of 20–25 g. of sodium bisulfite in 1 l. of water (Note 3). This procedure removes the excess iodine and precipitates the diphenylacetic acid as a fine white or slightly yellow powder (Note 4). The product is filtered with suction, washed with cold water and dried thoroughly on filter paper. The yield is 88–90 g. (94–97 per cent of the theoretical amount) of a solid melting at 141–144° (Note 5). If a crystalline product is desired, the acid is dissolved in about 500 cc. of hot 50 per cent alcohol and then cooled. The melting point after recrystallization is 144–145°.

### 2. Notes

1. In place of phosphorus, iodine and water, a dilute solution of hydriodic acid and phosphorus may be used.

2. If difficulties are encountered in filtering the hot acetic acid solution through filter paper, an asbestos filter may be prepared and used to advantage.

3. Some samples of sodium bisulfite caused part of the diphenylacetic acid to dissolve. This can always be avoided if, after the solution of sodium bisulfite is prepared, a current of sulfur dioxide is passed in, until the solution is acid to litmus.

4. Sometimes, if the acetic acid solution is poured into the water too rapidly, the product will be slightly pink and a reprecipitation from acetic acid solution will be necessary.

5. The melting points of benzilic acid and diphenylacetic acid lie very close together. However, it is very easy to test for complete reduction by treating a little of the product with cold concentrated sulfuric acid. If even a trace of benzilic acid remains the sulfuric acid will turn red.

### 3. Other Methods of Preparation

Diphenylacetic acid has been obtained by the reduction of benzilic acid with hydriodic acid and red phosphorus;[1] by the treatment of phenylbromoacetic acid with benzene and zinc dust,[2] or with benzene and aluminum chloride;[3] by the hydrolysis of diphenylacetonitrile;[4] by heating $\alpha$-diphenyldichloroethylene with alcoholic sodium ethylate;[5] by heating benzilic acid;[6] from diphenylmethane, mercury diethyl, sodium and carbon dioxide;[7] by the oxidation of $\alpha,\alpha,\delta,\delta$-tetraphenyl-$\beta$-butine;[8] by the decomposition of some complex derivatives obtained from diphenylketene;[9] by the hydrolysis of diphenyl-5,5-hydantoin;[10] by the treatment of diphenylbromoacetic acid with copper;[11] by the oxidation of dichlorodiphenylcrotonic acid.[12]

[1] Ann. **155**, 84 (1870); **275**, 84 (1893); Ber. **24**, 3556 (1891); **44**, 442 (1911).
[2] Ann. **171**, 122 (1874).
[3] Chem. Weekblad **5**, 655 (1908).
[4] Bull. soc. chim. (2), **33**, 590 (1880); Ann. **233**, 349 (1886).
[5] Ann. **306**, 81 (1899).
[6] Ann. **298**, 242 (1897); Ber. **40**, 4060 (1907).
[7] Ber. **43**, 1942 (1910).
[8] Z. Electrochem. **16**, 671 (1910).
[9] Ber. **42**, 4261 (1909); **44**, 523, 531 (1911).
[10] Ber. **46**, 139 (1913).
[11] Ann. **396**, 262, footnote 1 (1913).
[12] Am. Chem. J. **19**, 644 (1897).

# XIV

# EPICHLOROHYDRIN

$$CH_2Cl \cdot CHOH \cdot CH_2Cl + NaOH \rightarrow$$
$$H_2O + (CH_2Cl \cdot CHONa \cdot CH_2Cl) \rightarrow CH_2Cl \cdot \overbrace{CH - CH_2}^{O} + NaCl$$

Prepared by H. T. CLARKE and W. W. HARTMAN.
Checked by ROGER ADAMS and H. O. CALVERY.

## 1. Procedure

IN a 5-l. flask (Note 1) provided with a mechanical stirrer, a reflux condenser, and a hopper which can be opened or closed at the bottom by means of a rubber bung attached to a glass rod

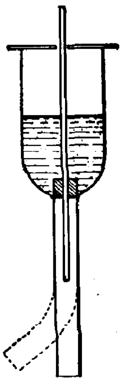


FIG. 2.

(Fig. 2), are placed 3 l. of anhydrous ether and 1290 g. of glycerol $\alpha,\gamma$-dichlorohydrin (Vol. II, p. 29). The flask is surrounded by a cold water bath, and 440 g. of finely powdered sodium hydroxide (Note 2), which has been passed through a 20-mesh sieve, is added in small portions, with continual stirring, while the temperature is kept at 25–30°. The addition requires about

twenty minutes. The cold water is replaced by water at 40–45°, and the mixture boiled gently with stirring for four hours. It is necessary to cool the vessel at least once every hour during this period and break up with a rod or wire (Note 3) any lumps which cling to the side of the flask and are not incorporated by the stirrer.

The mixture is finally cooled and the ethereal solution carefully decanted from the solid, which is carefully rinsed twice with 250 cc. portions of dry ether. The united liquids are then distilled from a water bath held at 40–60°, the residue is fractionated with a column, and the fractions boiling at the following points are collected: up to 110°; at 110–115°; at 115–117°; and at 117–140°. The portion boiling at 115–117° is pure epichlorohydrin; the lower and higher fractions are systematically redistilled, yielding a further quantity of pure material. The yield is 705–747 g. (76–81 per cent of the theoretical amount). The residue, varying from 16 to 150 g., consists of nearly pure glycerol dichlorohydrin, and may be employed in subsequent runs (Note 4).

## 2. Notes

1. A flask fitted with three necks (Vol. I, p. 12) is very satisfactory for this reaction; if it be not available, the tubes leading from the reflux condenser and the hopper must be bent at slight angles to prevent congestion of apparatus.

2. The principal difficulties in the preparation are connected with the use of finely powdered alkali. Care must be taken to expose the powder as little as possible to a moist atmosphere, for if it becomes at all damp it tends to clump together and difficulty is experienced in adding it to the mixture. For this reason, and also on account of the irritating action of alkali on the mucous membranes, the sieve should be provided with well-fitting cover and receiver; the sifted material should be weighed out into a stoppered bottle and placed in the apparatus directly from this container. The hopper from which the alkali is added to the mixture should be covered with a card with a hole through

which the rod passes. The bung on the rod may conveniently be constructed from a rubber stopper of appropriate size.

3. As stated by Claus,[1] the action of alkalies, whether solid or in aqueous or alcoholic solution, causes the formation of a considerable proportion of glycerol. This by-product, although formed to a markedly less extent when the reaction is carried out in ether, tends to coagulate the alkali and salt, so that it is essential to loosen the mass occasionally by poking it with a rod. Ether was selected as a diluent since it was hoped that in a non-hydroxylic medium the first stage of the reaction—replacement of hydrogen by sodium—would take place to a greater extent than if water or other hydroxylic liquid, such as alcohol or the dichlorohydrin itself, were employed. This is probably the case, since Claus found in an extensive series of experiments that the yield never rose above 42 per cent of that theoretically possible, even when solid alkali was employed without a diluent.

4. It is not essential to redistil the recovered dichlorohydrin, since the glycerol which forms the principal by-product is retained by the excess alkali and does not enter the ether.

## 3. Other Methods of Preparation

The only methods which come into consideration depend upon the action of alkalies upon glycerol $\alpha$- or $\beta$-dichlorohydrins.[1, 2]

[1] Ber. **10**, 557 (1877).
[2] Ann. Suppl. **1**, 221 (1861); Z. **1871**, 252; J. prakt. Chem. (2) **12**, 160 (1875).

# XV

## ETHYL β-BROMOPROPIONATE

$$CH_2Br \cdot CH_2 \cdot CO_2H + C_2H_5OH \rightarrow CH_2Br \cdot CH_2 \cdot CO_2C_2H_5 + H_2O$$

Prepared by E. C. Kendall and B. McKenzie.
Checked by H. T. Clarke and M. R. Brethen.

### 1. Procedure

To the crude mixture of ammonium bromide and β-bromopropionic acid, prepared as described on p. 25, from 317 g. of ethylene cyanohydrin, are added 1200 cc. of carbon tetrachloride and 200 cc. of the same solvent which has been shaken with the aqueous distillates; the ammonium bromide is filtered off and washed with 200 cc. of carbon tetrachloride. The watery layer, amounting to about 350 cc., is separated and shaken with 100 cc. of carbon tetrachloride. To the united carbon tetrachloride solutions are added 450 cc. of 95 per cent ethyl alcohol and 10 g. of sulfosalicylic acid or phenolsulfonic acid to act as a catalyst (Note 1).

The mixture is now boiled in a 3-l. flask, the vapors being passed through an efficient condenser and the condensed liquid run into an automatic separator (see Vol. I, p. 68) so arranged that the heavy liquid is returned to the flask and the lighter aqueous liquid discarded. If the boiling is sufficiently vigorous no more water will separate after two to two and a half hours' boiling (Note 2). The reaction mixture is now cooled, washed with dilute sodium carbonate solution, and distilled with the use of a column until the temperature of the vapor reaches 85° and that of the liquid in the flask about 115°. The residue is then transferred to a flask provided with a column for distillation under reduced pressure (see Vol. I, p. 30) and distilled. The fraction boiling at 60–65°/15 mm. is collected, 690–700 g. of

pure ethyl β-bromopropionate being obtained (85–87 per cent of the theoretical amount). A high-boiling residue, probably consisting of ethyl hydracrylate, remains in the flask, but the amount is practically negligible.

## 2. Notes

1. The esterification may be carried out without the addition of a sulfonic acid, as traces of hydrobromic acid generally remain in the crude material; but since the time of operation must be kept as short as possible this omission is not recommended. It has been found that if the water be not removed and the mixture boiled under a reflux condenser for two hours before the distillate is passed through the automatic separator, the yield falls to 70–75 per cent of the theoretical amount.

2. It is important to carry out the esterification as rapidly as possible in order to cut down to a minimum the formation of ethyl hydracrylate, which takes place by the action of water on the β-bromopropionic acid or ester; an efficient condenser is therefore necessary. For the same reason it is necessary to remove all residual water from the mixture before adding the alcohol.

3. As in the preparation of the β-bromopropionic acid, benzene must not be substituted for the carbon tetrachloride, as it has been found impossible to make a satisfactory separation of this solvent from the ester.

## 3. Other Methods of Preparation

Ethyl β-bromopropionate has always been prepared by the esterification of β-bromopropionic acid.[1]

[1] J. prakt. Chem. (2) **42**, 384 (1890); Compt. rend. **118**, 1268 (1894).

# XVI

## ETHYL CYANOACETATE

$$Cl \cdot CH_2 \cdot CO_2Na + NaCN \rightarrow CN \cdot CH_2 \cdot CO_2Na + NaCl$$
$$CN \cdot CH_2 \cdot CO_2H + C_2H_5OH \rightarrow CN \cdot CH_2 \cdot CO_2C_2H_5 + H_2O$$

Prepared by E. P. KOHLER and C. F. H. ALLEN.
Checked by C. S. MARVEL and H. O. CALVERY.

### 1. Procedure

A mixture of 625 g. of chloroacetic acid and 940 g. of cracked ice in a large battery jar is accurately neutralized to litmus with a cold solution of sodium hydroxide containing 333 g. per l.; about 825 cc. is required. The temperature must not be allowed to rise above 30° during the neutralization.

A solution is now made (in the hood) of 387.5 g. of sodium cyanide (1.174 mol.) in 780 cc. of water. This is heated, gently at first to induce rapid solution, and finally to boiling. To the hot solution is added 300 cc. of the sodium chloroacetate solution, and the flame is removed as soon as the action begins. When the vigorous reaction has subsided somewhat, another 300-cc. portion is added; this is continued until all has been added. The mixture is then boiled for five minutes, and finally cooled under the tap for half an hour (Note 1).

To the solution (in the hood) is added slowly, with stirring, 767 cc. of 43 per cent sulfuric acid (sp. gr. 1.333), or its equivalent of about this concentration. Some hydrogen cyanide is evolved from the excess cyanide present. The volume is now 4400 cc. The mixture is left to stand for five minutes to allow any salts to precipitate, and filtered in a centrifuge or by suction, the salt being saved for future use. The aqueous solution is evaporated under diminished pressure, using a 2-l. Pyrex distilling flask fitted with a dropping funnel and a capillary tube for

admitting air below the surface of the liquid. The receiver consists of two 1-l. suction flasks in series in an ice bath. The distilling flask is immersed in a hot-water bath, the temperature of which is not allowed to rise above 80° (Note 2); 500 cc. of the solution is put in the flask and distillation commenced, the remainder of the solution being added from the dropping funnel as fast as it will distil. The flask should be shaken if bumping occurs on account of the separated salt. Heating is continued until no more distillate is obtained; the time required amounts to about eight hours.

While the distillation is proceeding the salt is washed in the centrifuge or on the funnel with 95 per cent ethyl alcohol, first with two 100-cc. portions and finally with one of 200 cc. The salt is discarded, and the filtrate added to the residue in the distilling flask while it is still warm, the whole being shaken to prevent a solid cake from forming. After it has been thoroughly shaken in order to break up any lumps, the salt in the distilling flask is filtered off or centrifuged and washed as before, twice with 100-cc. portions of 95 per cent ethyl alcohol and finally with one of 280 cc. The salt, which should be nearly dry, is discarded; the alcoholic filtrate is distilled under reduced pressure from a water bath held at 60° (Note 2), continuing as long as any liquid comes over (about three hours). Alcohol may be recovered from the distillate.

The residual liquid is carefully decanted from any salt into a 2-l. round-bottom flask, and rinsed carefully with 300 cc. of absolute ethyl alcohol. The cyanoacetic acid so obtained is esterified by passing the vapor of ethyl alcohol into the hot solution. The apparatus for esterification is arranged as follows: a rubber stopper to fit the 2-l. flask containing the acid is bored for (*a*) a fractionating column connected with a condenser set for downward distillation, (*b*) a thermometer, the bulb of which dips into the liquid, (*c*) a glass tube reaching to the bottom of the flask, drawn out into a large capillary. A 1-l. Pyrex round-bottom flask is fitted with a stopper carrying (*a*) a dropping funnel, (*b*) a safety tube (to release pressure, if necessary), and (*c*) a bent glass tube to conduct the alcohol vapor through a

trap to the capillary glass tube in the reaction flask. The purpose of the trap is to catch any liquid that may be sucked back from the reaction flask.

To the reaction mixture is added 15 cc. of concentrated sulfuric acid and the flask is placed in an oil bath; connections are made to the rest of the apparatus and heating is commenced. About 70 cc. of alcohol will distil over before the temperature of the mixture reaches 110°. Meanwhile, 600 cc. of 95 per cent ethyl alcohol is placed in the 1-l. flask. As soon as the temperature reaches 110° this alcohol is boiled so that a rapid stream of vapor passes into the reaction mixture—the temperature should remain at 110°. More alcohol is added to that in the 1-l. flask until 800 cc. has been added; heating is continued until all has been vaporized, whereupon the safety tube is opened at once. The flask is removed from the oil bath and allowed to cool. This esterification takes about three hours. The distillate obtained during the process consists of dilute alcohol.

When the ester has cooled to room temperature, the sulfuric acid is neutralized with a strong solution of sodium carbonate; the ester (upper layer) is separated, and the aqueous solution extracted with ether, or preferably benzene; about one-tenth of the yield is in the extract. The combined products are placed in a 1-l. vacuum distillation flask and distilled under reduced pressure, after the bulk of the solvent and accompanying alcohol and water has been removed. When the temperature of the distillate reaches 94°/16 mm. the receiver is changed, and the ester collected from 94° to 99°, most of it coming over at 97–98°/16 mm. (Note 3). The temperature of the oil bath should not rise above 145°. A small amount (about 60 g.) of residue remains in the flask. The yield is 490–550 g. (65–75 per cent of the theoretical amount). The total time necessary for the preparation of this quantity of ester is about twenty-four hours.

## 2. Notes

1. The reaction between sodium chloroacetate and sodium cyanide should take place quickly; the solution should not be boiled more than five minutes.

2. The solution containing mineral acid must not be evaporated at a high temperature, or ethyl malonate will be formed.

3. Ethyl cyanoacetate boils at 97°/16 mm., 101°/19 mm., 107°/27 mm. A very small amount of white solid sometimes appears in the distillate; this will settle out or may be filtered off.

4. Methyl cyanoacetate can also be made by this method, if methyl alcohol be used instead of ethyl alcohol.

### 3. Other Methods of Preparation

Ethyl cyanoacetate has been prepared by the action of potassium cyanide on ethyl chloroacetate,[1] and by the esterification of cyanoacetic acid.[2]

[1] Ann. **133**, 339 (1865); Jahresb. **1874**, 561; Bull. soc. chim. **46**, 62 (1886); J. Am. Chem. Soc. **26**, 1545 (1904); Proc. Chem. Soc. **30**, 307 (1914).

[2] Am. J. Sci. **26**, 267 (1908).

# XVII

## ETHYLENE CYANOHYDRIN

$$CH_2OH \cdot CH_2Cl + NaCN \rightarrow CH_2OH \cdot CH_2 \cdot CN + NaCl$$

Prepared by E. C. KENDALL and B. MCKENZIE.
Checked by H. T. CLARKE and W. M. SPERRY.

### 1. Procedure

IN a 5-l. flask is placed 612 g. of finely powdered sodium cyanide (passed through a meat grinder and then sifted through a 20-mesh sieve); the flask is equipped with a thermometer in a well, an efficient stirrer, and a reflux condenser (Note 4). The whole vessel is then set in a water bath into which warm and cold water can be run at will and if necessary rapidly removed.

A mixture of 250 cc. of water and 1000 g. of pure ethylene chlorohydrin (b. p. 126–127°) is then added, the stirring is started, and the temperature of the mixture raised to 45° by external application of warm water. At this point the warm water is rapidly removed (Note 2) and the temperature of the contents of the flask carefully held at 45° by jacketing with water at a suitable temperature (33–35°). After the mixture has been held at 45° for an hour it is allowed to warm up to 48° by allowing the temperature of the water bath to rise two degrees. After an hour at 48° the temperature is raised to 50° and held at this point until the reaction is over; it is necessary to raise the temperature of the bath gradually, and the end of the reaction is noted when the bath temperature reaches 50°. A period of four and a half to five hours is necessary for this last stage.

Cold water is now placed in the water bath, while the stirrer is kept always in motion, and the temperature of the mixture is reduced to 20–22°. The mass is then filtered by suction and the sodium chloride sucked as dry as possible. This is then washed

with about 800 cc. of acetone in small quantities, the washings being collected separately, and then transferred to a flask from which the acetone and water are distilled off with the use of a short fractionating column until the temperature of the vapor reaches 90°. The residue in the flask is then cooled and again filtered from a further small quantity of sodium chloride which separates during the distillation, the filtrate being added to the main product.

This is then distilled under reduced pressure from an oil bath, and the fraction boiling at 107–109°/12 mm. (116–118°/20 mm.) is collected as pure material. The yield is 700–705 g. (79–80 per cent of the theoretical amount). There is practically no residue beyond a little salt; the foreruns consist of water, a small amount of unchanged ethylene chlorohydrin and some ethylene cyanohydrin.

## 2. Notes

1. The sodium cyanide should be finely powdered since it never completely enters into solution, and any lumps present would run the risk of becoming coated over with sodium chloride. For the same reason, the stirring must be vigorous throughout the operation.

2. It is most important that the temperature of the reaction mixture be not allowed to rise prematurely, since if it reaches 50° during the early stages the reaction velocity increases so rapidly that the contents are apt to boil out of the flask. For the same reason it appears necessary that a certain ratio between reacting mass and cooled surface be not exceeded. Runs of twice the above size have been carried out in a 5-l. flask without mishap, but temperature control was difficult and these conditions are extremely hazardous. A run of 4 kg. of ethylene chlorohydrin in a 12-l. flask was attempted, but rapidly went out of control.

3. When the reaction has been carried out exactly as described, the final product before distillation is very nearly colorless; if the temperature has been allowed to rise too high,

a brown color is produced and ammonia is formed, with corresponding loss of yield.

4. Under the correct conditions no appreciable amount of hydrogen cyanide escapes from the reflux condenser, but it is wise to carry out the reaction under a hood or to lead a tube from the top of the condenser into the open air.

### 3. Other Methods of Preparation

Ethylene cyanohydrin has been prepared by the action of ethylene oxide upon anhydrous hydrocyanic acid;[1] but the majority of methods described in the literature have involved the interaction of ethylene chlorohydrin and alkali cyanide. This has been effected in the absence of a solvent by heating to 100° in a closed vessel,[2] by boiling the reagents in 50 per cent aqueous-alcoholic solution,[3] by adding a concentrated aqueous solution of potassium or sodium cyanide to a boiling solution of ethylene chlorohydrin in absolute alcohol,[4] and in aqueous solution at 45°.[5]

[1] Ann. **191**, 270 (1878); *cf.* Ann. **167**, 346 (1873).

[2] Ann. **128**, 4 (1863).

[3] Ann. **191**, 268 (1878).

[4] Bull soc. chim. (3) **9**, 426 (1893); *ibid.* (4) **27**, 902 (1920); J. Am. Chem. Soc. **39**, 1465 (1917).

[5] U. S. Patent 1,388,016; C. A. **15**, 4011 (1921).

XVIII

## HYDROXYLAMINE HYDROCHLORIDE AND ACETOXIME

$$NaNO_2 + NaHSO_3 + SO_2 \rightarrow HON(SO_3Na)_2$$
$$HON(SO_3Na)_2 + CO(CH_3)_2 + H_2O \rightarrow HON{=}C(CH_3)_2 + 2NaHSO_4$$
$$HON{=}C(CH_3)_2 + HCl + H_2O \rightarrow HONH_2 \cdot HCl + CO(CH_3)_2$$

Prepared by WALDO L. SEMON.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

IN a 2-gallon wide-mouth bottle packed in ice-salt mixture are placed 630 g. of commercial (95 per cent) sodium nitrite and 5 kg. of chopped ice, and the mixture is well stirred. A cold (0–5°) solution of sodium bisulfite, made by saturating with sulfur dioxide a solution of 495 g. of anhydrous sodium carbonate in 1500 cc. of water, is now added slowly with hand stirring. When all is in, a sufficiently large quantity of the ice will have melted to allow a mechanical stirrer to be fitted. A stream of sulfur dioxide is now passed in, with continual stirring, the temperature being kept at 0–2°, until an acid reaction to Congo red paper is obtained and the dark color, which appears just before the reaction is complete, has faded. During the addition of the sulfur dioxide, 500 g. more of ice may be added.

The mixture is now transferred to a 12-l. flask, 625 cc. (495 g.) of acetone is added, and the solution is heated on the steam bath to 70°. Heating is then discontinued, the flask wrapped in burlap in order to retard loss of heat, and the mixture allowed to stand over night. The acid is then neutralized with a concentrated (50 per cent) solution of sodium hydroxide (about 720 g. of alkali is required), a distinctly alkaline reaction to litmus being just obtained.

The resulting acetoxime is now distilled out in a current of steam (Note 2), and the distillation is continued until a 5-cc. sample, shaken out with 2 cc. of ether, yields no appreciable residue on evaporating the ether. To the distillate (2–2.5 l.) is added 600 cc. of concentrated hydrochloric acid, and the acid solution is distilled at atmospheric pressure until the distillate is free of acetone. The residual liquor is then evaporated to dryness on the steam bath, either in an open dish or preferably under reduced pressure; the crude hydroxylamine hydrochloride so obtained, weighing 296–470 g. (49–77 per cent of the theoretical amount) is suitable for many purposes, but is best purified by recrystallization from half its weight of water. By systematic recrystallization of the product from several batches, the yield of pure product, which crystallizes in long flat needles, melting when dry at 150–151°, may be brought as high as 70 per cent of the theoretical amount (Note 3).

In order to prepare pure acetoxime (Note 4), the procedure is modified in the following way: After neutralizing the solution of acetoxime formed after the addition of acetone, the oily layer is separated and the aqueous solution shaken with two or three 150-cc. portions of benzene. The oil and benzene solutions are mixed, the water thereby thrown out is removed, and the oil fractionally distilled with the use of a column, the portion boiling 133–136° being collected as pure acetoxime. This product, which weighs 420–480 g., solidifies in the receiver to colorless needles melting at 60–61°. The foreruns and aqueous liquors are best distilled with steam and the distillate converted into hydroxylamine hydrochloride as above, whereupon 75–90 g. of pure salt is obtained.

## 2. Notes

1. The preparation can be run in larger batches than that indicated above. Earthenware crocks may suitably replace the glass bottle; but since the external cooling in such vessels is not so efficient, it will be necessary, in case they are used, to add a larger proportion of ice during the reaction in order to maintain the correct temperature. This, however, is of no great disadvan-

tage, since the formation of the oxime appears to take place equally well in more dilute solution. Metal cans are entirely satisfactory for the distillation of the faintly alkaline liquors.

2. The acetoxime may be distilled by direct heating rather than by injection of steam; when the prescribed quantities are taken, however, it will be found that the liquor becomes saturated with sodium sulfate at a point just before the expulsion of the oxime is complete, so that addition of water during the distillation is necessary. More rapid distillation can be obtained by the use of a current of steam, especially if a condensing receiver (Vol. II, pp. 80–82) be employed. The oxime can also, if desired, be isolated for hydrolysis by separation of the oily layer and extraction with benzene; the resulting crude hydroxylamine hydrochloride is, however apt to be dark in color and to contain inorganic salts.

3. The final mother liquors from the recrystallization of the hydroxylamine hydrochloride contain a high proportion of ammonium chloride. The hydroxylamine present therein is best recovered by reconversion into acetoxime, which is isolated by steam distillation of the faintly alkaline solution.

4. Acetoxime can be obtained in long needles by allowing the first portions of the steam distillate (which are saturated with oxime) to cool, and filtering off the crystals which separate; unfortunately, this product cannot be obtained in a perfectly dry condition without considerable loss by volatilization.

5. By redistillation of the aqueous acetone with the use of a column, 60 per cent or more of the material taken can readily be recovered and employed in a subsequent batch.

## 3. Other Methods of Preparation

Hydroxylamine hydrochloride was first prepared [1] by the reduction of ethyl nitrate by means of tin, with hydrochloric acid; hydroxylamine salts have also been prepared by the reduction of nitric acid with metals.[2] The two important

[1] Ann. Suppl. **6**, 220 (1868).

[2] J. Chem. Soc. **43**, 443 (1883); **47**, 597 (1885); **75**, 87 (1899); J. Soc. Chem. Ind. **14**, 595 (1895).

technical methods consist in the electrolytic reduction of nitric acid [3] and the action of sodium bisulfite upon sodium nitrite.[4] Raschig, who discovered the latter process for the preparation of hydroxylamine sulfate, has suggested the use of calcium nitrite and bisulfite, so that the bulk of the inorganic salts can be removed in the form of calcium sulfate.[5] The same chemist also showed that sodium hydroxylaminedisulfonate yields acetoxime on treatment with acetone,[6] and it has long been known that acetoxime readily yields hydroxylamine hydrochloride on treatment with hydrochloric acid; [7] but advantage appears only recently [8] to have been taken of these facts in combination.

[3] Zeit. anorg. Chem. **31**, 322 (1902); D. R. P. 133,457 (1902), Chem. Zentr. **1902** (ii), 313; D. R. P. 137,697 (1903), Chem. Zentr. **1903** (i), 106.

[4] Ann. **241**, 161 (1887); D. R. P. 41,987 (1887), J. Chem. Soc. **54**, 913 (1888); J. Chem. Soc. **69**, 1665 (1896); **77**, 673 (1900); J. Am. Chem. Soc. **40**, 1281 (1918).

[5] D. R. P. 216,747 (1910), Chem. Zentr. **1910** (i), 308.

[6] Ann. **241**, 187 (1887).

[7] Ber. **16**, 170 (1883).

[8] J. Am. Chem. Soc. **45**, 188 (1923).

## XIX

## MERCURY DI-*p*-TOLYL

$$2CH_3 \cdot C_6H_4 \cdot HgCl + 4NaI \rightarrow (CH_3 \cdot C_6H_4 \cdot)_2Hg + 2NaCl + Na_2HgI_4$$

Prepared by F. C. WHITMORE, N. THURMAN, and FRANCES H. HAMILTON.
Checked by J. B. CONANT and F. C. WHIDDEN.

### 1. Procedure

IN a 2-l. round-bottom flask fitted with a reflux condenser and an efficient glass stirrer, are placed 700 cc. of 95 per cent ethyl alcohol, 100 g. of recrystallized *p*-tolylmercuric chloride (p. 99), and 160 g. of sodium iodide (80 per cent excess). This mixture is boiled with vigorous stirring (Note 2) for fifteen hours; the solid does not entirely enter into solution at any time. The mixture is then thoroughly cooled and filtered by suction and the solid washed with water until free of inorganic halide. It is then dried in an air-oven at 40° and recrystallized from 500 cc. of boiling xylene (Note 3). In this way 45–50 g. (78–85 per cent of the theoretical amount) of a product melting at 238° is obtained.

### 2. Notes

1. Mercury compounds of the type R.Hg.X can be changed to those of the type $R_2Hg$, by almost any neutral or alkaline reagent which tends to change mercuric ions to metallic mercury or to a stable complex ion. Some of these reagents are inorganic iodides, thiocyanates, thiosulfates, sulfides, hydrosulfites, ferrous hydroxide, sodium amalgam, metallic sodium, and sodium stannite. Preliminary experiments indicated that potassium thiocyanate was the best reagent for preparing the mercury

ditolyl, but it was later found that the use of sodium iodide with vigorous stirring gave even better results.

2. Stirring decreases the time required for the reaction and increases the yield. Without stirring it is practically impossible to obtain a product which is free from halogen.

3. Since the mercury ditolyl has practically the same solubility in xylene as the tolylmercuric iodide and chloride, the latter will be present in the recrystallized product if the reaction has not gone to completion. A trace of unchanged product may readily be detected by the metallic sodium test for inorganic halides.

## 3. Other Methods of Preparation

Mercury di-*p*-tolyl has also been prepared by boiling *p*-bromotoluene with sodium amalgam in xylene in the presence of ethyl acetate as a catalyst.[1]

[1] Ann. **154**, 171 (1870); Compt. rend. **68**, 1298 (1869); Ann. **201**, 246 (1880).

# METHYLAMINE HYDROCHLORIDE

$$2HCHO + NH_4Cl \rightarrow CH_3NH_2 \cdot HCl + HCO_2H$$

Prepared by C. S. Marvel and R. L. Jenkins.
Checked by J. B. Conant and F. C. Whidden.

## 1. Procedure

In a 5-l. round-bottom flask fitted with a stopper holding a condenser set for downward distillation and a thermometer which will extend well into the liquid, are placed 4000 g. of technical formaldehyde (35–40 per cent; sp. gr. 1.078 at 20°) and 2000 g. of technical ammonium chloride. The mixture is heated on the steam bath until no more distillate comes over and then over a flame until the temperature of the solution reaches 104°. The temperature is held at this point until no more distillate comes over (four to six hours). The distillate, which consists of methylal, methyl formate and water, may be treated as described in Note 3.

The contents of the reaction flask are cooled to room temperature (Note 1), and the ammonium chloride which separates is filtered off and centrifuged (Note 2). The mother liquor is concentrated on the steam bath under reduced pressure to 2500 cc., and again cooled to room temperature, whereupon a second crop of ammonium chloride is obtained. The total recovery of ammonium chloride up to this point amounts to 780–815 g.

The mother liquor is again concentrated under reduced pressure until crystals begin to form on the surface of the solution (1400–1500 cc.). It is then cooled to room temperature and a first crop of methylamine hydrochloride, containing some ammonium chloride, is obtained by filtering the cold solution

and centrifuging the crystals (Note 2). At this point 625–660 g. of crude product is obtained. The mother liquor is now concentrated under reduced pressure to about 1000 cc. and cooled, a second crop of methylamine hydrochloride (170–190 g.) is then filtered off and centrifuged. This crop of crystals is washed with 250 cc. of cold chloroform, filtered and centrifuged, in order to remove most of the dimethylamine hydrochloride which is present; after the washing with chloroform the product weighs 140–150 g. The original mother liquor is then evaporated under reduced pressure, as far as possible, by heating on a steam bath, and the thick syrupy solution (about 350 cc.) which remains is poured into a beaker and allowed to cool, with occasional stirring, in order to prevent the formation of a solid cake (Note 1). The thick paste so obtained is centrifuged, and the crystals (170–190 g.) are washed with 250 cc. of cold chloroform; the solution is filtered and the crystals are centrifuged, thus yielding 55–65 g. of product. There is no advantage in further concentrating the mother liquor.

The total yield of crude centrifuged methylamine hydrochloride is 830–850 g. This product contains, as impurities, water, ammonium chloride, and some dimethylamine hydrochloride. In order to obtain a pure product, the crude methylamine hydrochloride is recrystallized from absolute alcohol (Note 4). The crude salt is placed in a 5-l. round-bottom flask fitted with a reflux condenser protected at the top with a calcium chloride tube; 2 l. of absolute alcohol is added and the mixture heated to boiling. After about half an hour the undissolved material is allowed to settle and the clear solution is poured off. When the alcoholic solution is cooled, methylamine hydrochloride crystallizes out. It is filtered off and centrifuged, and the alcohol used for another extraction. The process is repeated until the alcohol dissolves no more of the product (about five extractions are necessary). In the flask 100–150 g. of ammonium chloride remains, making the total recovery of ammonium chloride 850–950 g. The yield of recrystallized methylamine hydrochloride is 600–750 g. (45–51 per cent of the theoretical amount, based on the ammonium chloride used up in the process).

## 2. Notes

1. The methylamine hydrochloride solutions should be cooled rapidly in order to bring the salt down in small crystals which may be easily purified.

2. Centrifuging the precipitates is the only satisfactory method of drying, as all of the products tend to take up water when allowed to stand in the air.

3. Methylal and sodium formate may be obtained from the first distillate of the main reaction mixture. The crude distillate is placed in a flask fitted with a reflux condenser and to it is added a solution of 200 g. of sodium hydroxide in 300 cc. of water. The methyl formate is hydrolyzed to sodium formate. The methylal layer is separated, dried over calcium chloride and distilled. In this way 240–260 g. of methylal, boiling at 37–42°, is obtained. By evaporating the watery portion to dryness there is obtained a residue of about 280 g. of crude sodium formate.

4. Since ammonium chloride is not absolutely insoluble in 100 per cent ethyl alcohol (100 g. dissolve 0.6 g. at 15°) the methylamine hydrochloride purified in the manner described contains appreciable traces of it. A purer product can be prepared by recrystallizing from *n*-butyl alcohol, in which the solubility of ammonium chloride even at the boiling temperature is negligibly small. Methylamine hydrochloride is somewhat less soluble in this solvent than in ethyl alcohol, but as a rule three extractions carried out at 90–100° with 4–6 parts of fresh butyl alcohol for each extraction result in a substantially complete separation. Since the last traces of the solvent are not readily removed by exposure to air, a solution of the recrystallized material in a small quantity of water should be distilled until free of alcohol, and allowed to crystallize.

5. The literature[1] claims a yield of methylamine hydrochloride amounting to 79 per cent of the weight of ammonium chloride used up in the reaction. This figure is probably based

[1] J. Chem. Soc. **111**, 850 (1917).

on the weight of crude methylamine hydrochloride and not of the recrystallized material.

### 3. Other Methods of Preparation

Methylamine occurs in herring brine;[2] in crude methyl alcohol from wood distillation,[3] and in the products obtained by the dry distillation of beet molasses residues.[4] It has been prepared synthetically by the action of alkali on methyl cyanate or iso-cyanurate;[5] by the action of ammonia on methyl iodide,[6] methyl chloride,[7] methyl nitrate,[8] or dimethyl sulfate;[9] by the action of methyl alcohol on ammonium chloride,[10] on the addition compound between zinc chloride and ammonia,[11] or on phospham;[12] by the action of bromine and alkali on acetamide;[13] by the action of sodamide on methyl iodide;[14] by the reduction of chloropicrin,[15] of hydrocyanic or of ferrocyanic acid,[16] of hexamethylenetetramine,[17] of nitromethane,[18] or of methyl nitrite;[19] by the action of formaldehyde on ammonium chloride.[20]

[2] Ber. **18**, 1922 (1885).

[3] Jahresb. **1873**, 686; Ann. chim. phys. (5) **1**, 444 (1874).

[4] Ann. chim. phys. (5) **23**, 316 (1881).

[5] Ann. **71**, 332 (1849).

[6] Ann. **79**, 16 (1851).

[7] Bull. soc. chim. **45**, 499 (1886).

[8] Compt. rend. **48**, 344 (1859); Ann. **110**, 255 (1859); Jahresb. **1862**, 327; Ann. chim. phys. (5) **23**, 321 (1881).

[9] Ber. **43**, 139 (1910); J. Chem. Soc. **117**, 236 (1920).

[10] Ber. **8**, 458 (1875).

[11] Ber. **17**, 639 (1884).

[12] D. R. P. 64,346, Frdl. **3**, 13 (1890–94).

[13] Ber. **15**, 765 (1882); Compt. rend. **147**, 430, 680, 983 (1908).

[14] Compt. rend. **156**, 328 (1913).

[15] Ann. **109**, 282 (1859); **184**, 51 (1877); J. Chem. Soc. **115**, 159 (1919).

[16] Ann. **121**, 139 (1862); **128**, 201 (1863); Z. physik. Chem. **72**, 674 (1910); D. R. P. 264,528, Frdl. **11**, 110 (1912–14).

[17] D. R. P. 73,812, Frdl. **3**, 15 (1890–94); Bull. soc. chim. (3) **11**, 23 (1894); D. R. P. 143,197, Frdl. **7**, 24 (1902–04); D. R. P. 148,054, Frdl. **7**, 26 (1902–04); C. A. **9**, 2232 (1915).

[18] Bull. soc. chim. (3) **21**, 783 (1899); (4) **7**, 954 (1910); Ber. **44**, 2403 (1911).

[19] Bull. soc. chim. (4) **7**, 824 (1910); Ann. chim. phys. (8) **25**, 136 (1912).

[20] Bull. soc. chim. (3) **13**, 534 (1895); Compt. rend. **147**, 429 (1908); J. Chem. Soc. **111**, 848 (1917); J. Am. Chem. Soc. **40**, 1411 (1918).

# XXI

## METHYL *m*-NITROBENZOATE

$$C_6H_5 \cdot CO_2CH_3 + HNO_3 \rightarrow NO_2 \cdot C_6H_4 \cdot CO_2CH_3 + H_2O$$

Prepared by Oliver Kamm and J. B. Segur.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure

Into a 2-l. round-bottom flask fitted with a mechanical stirrer, are placed 400 cc. of concentrated sulfuric acid cooled to 0°, and 204 g. (1.5 mols.) of pure methyl benzoate (Note 1). The mixture is cooled by means of an ice bath to 0–10° and then, with stirring, there is added gradually by means of a dropping funnel a mixture of 125 cc. concentrated nitric acid (sp. gr. 1.42) and 125 cc. concentrated sulfuric acid. During the addition of the nitrating acid, which requires about one hour, the temperature of the reaction mixture should be kept within the range 5–15° (Note 2).

After the nitric acid has been added, stirring is continued for fifteen minutes longer; the mixture is then poured upon 1300 g. of cracked ice. The crude methyl *m*-nitrobenzoate separates as a solid and is filtered off by means of suction and washed with water. The product is placed in a flask and agitated with 200 cc. of ice-cold methyl alcohol in order to remove a small amount of *o*-nitrobenzoic ester and other impurities that are present. The cooled mixture is then filtered by means of suction, washed with another 100-cc. portion of cold methyl alcohol (Note 3), and the solid dried. The yield is 220–230 g. (81–85 per cent of the theoretical amount) of an almost colorless product melting at 74–76°. In order to obtain a product of maximum purity, which melts at 78°, it is advisable to recrystallize the ester from an equal weight of methyl alcohol.

## 2. Notes

1. It is necessary that the methyl benzoate should be of high purity and dissolve in sulfuric acid without color. Commercial methyl benzoate which does not meet the latter specification may give yields about 10 per cent lower.

2. The nitration of methyl benzoate runs unusually smoothly, but it is essential to keep the temperature within the specified limits, otherwise the yield falls; at 50°, 193 g. of solid product is obtained, while at 70° the yield falls to 130 g.

3. On diluting the methyl alcoholic filtrate with water, 10–20 cc. of oil separates; more of this oil is formed by nitrating at higher temperatures, amounting to 57 cc. at 50° and 100 cc. at 70°. The oil consists not merely of methyl *o*-nitrobenzoate with some of the meta compound but contains also traces of dinitrobenzoic ester and nitrophenolic compounds. Unchanged methyl benzoate does not appear to be present.

4. The nitration method is also adaptable to the preparation of ethyl *m*-nitrobenzoate. The yield is, however, slightly lower, owing to the greater solubility of the ethyl ester.

## 3. Other Methods of Preparation

Methyl *m*-nitrobenzoate has been prepared by the esterification of *m*-nitrobenzoic acid;[1] this method is, however, obviously much less satisfactory than nitration of methyl benzoate. Nitration by means of fuming nitric acid has also been applied to methyl benzoate,[2] but the use of the ordinary nitration mixture of concentrated sulfuric acid and concentrated nitric acid is more satisfactory.

[1] Ann. **72**, 275 (1849).
[2] Rec. trav. chim. **17**, 97, 100 (1898).

## XXII

## *m*-NITROBENZOIC ACID

$$NO_2 \cdot C_6H_4 \cdot CO_2CH_3 + NaOH \rightarrow NO_2 \cdot C_6H_4 \cdot CO_2Na + CH_3OH$$
$$NO_2 \cdot C_6H_4 \cdot CO_2Na + HCl \rightarrow NO_2 \cdot C_6H_4 \cdot CO_2H + NaCl$$

Prepared by Oliver Kamm and J. B. Segur.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure

In a 2-l. round-bottom flask fitted with a reflux condenser are placed a solution of 80 g. (2 mols) of sodium hydroxide in 320 cc. of water (Note 1) and 180 g. (1 mol.) of methyl *m*-nitrobenzoate (not recrystallized, p. 71). The mixture is heated to boiling during five to ten minutes or until the saponification is complete as shown by the disappearance of the ester.

The reaction mixture is now diluted with an equal volume of water, and when cool is poured, with stirring, into 250 cc. of concentrated hydrochloric acid (Note 2). After the solution has cooled to room temperature, the *m*-nitrobenzoic acid is filtered off by means of suction. This crude acid when dry weighs 150–160 g. (87–93 per cent of the theoretical amount). It possesses a light brownish color, melts at 140°, and should be completely soluble in ether, thus showing the absence of salts. This acid is satisfactory for many purposes, but in order to prepare a perfectly pure product it must be crystallized once from 1 per cent aqueous hydrochloric acid. A light cream-colored product is thus obtained with a loss of about 5 per cent of the material.

### 2. Notes

1. The use of a more dilute sodium hydroxide solution than that recommended above has been found to yield unsatisfactory

results in the saponification of the ester. Prolonged boiling may lead to the production of colored products.

2. After the hydrolysis of the methyl *m*-nitrobenzoate it is essential that the solution of the sodium salt be poured into the acid. If acid be added to the salt in the usual way, a less soluble acid salt separates; and as this cannot be entirely removed from the *m*-nitrobenzoic acid even on long digestion with hydrochloric acid, a product is obtained which does not dissolve completely in ether.

3. *m*-Nitrobenzoic acid is soluble to the extent of 1 part in 300 parts of water at 20°, and 20 parts at 100°. The crystallization from water or dilute hydrochloric acid is therefore quite satisfactory.

4. *m*-Nitrobenzoic acid is obtained in a higher yield by nitration of methyl benzoate (p. 71) with subsequent hydrolysis than by the direct nitration of benzoic acid; this method is also preferable on account of the laborious nature of the methods necessary for the separation of the meta acid from the small quantities of the para isomer formed in the latter process.

### 3. Other Methods of Preparation

*m*-Nitrobenzoic acid has been prepared by the nitration of benzoic acid by means of nitric acid,[1] a mixture of nitric acid and sulfuric acid,[2] or mixtures of nitrates and sulfuric acid;[3] all of these methods lead to the production of a mixture containing principally the *m*-nitrobenzoic acid with a smaller proportion of *o*-nitrobenzoic acid and 1–2 per cent of *p*-nitrobenzoic acid, and the separation of these isomers is troublesome. *m*-Nitrobenzoic acid has also been prepared by the oxidation of the difficultly accessible *m*-nitrotoluene by means of chromic acid mixture[4] or permanganate.[5] It has also been formed by the nitration of hippuric acid with subsequent hydrolysis.[6]

[1] Ann. **34**, 297 (1840); Ann. **222**, 72 (1884).
[2] Ann. **91**, 186 (1854).
[3] Ann. **91**, 185 (1854); Ber. **10**, 862 (1877).
[4] Ann. **155**, 25 (1870).
[5] J. Am. Chem. Soc. **41**, 1569, (1919).
[6] Ann. **78**, 104 (1851).

XXIII

## *p*-NITROBENZOYL CHLORIDE

$$NO_2 \cdot C_6H_4 \cdot CO_2H + PCl_5 \rightarrow NO_2 \cdot C_6H_4 \cdot COCl + POCl_3 + HCl$$

Prepared by Roger Adams and R. L. Jenkins.
Checked by Oliver Kamm.

### 1. Procedure

In a 3-l. round-bottom flask are mixed 500 g. (1 mol.) of pure *p*-nitrobenzoic acid and 626 g. (1.05 mol.) of pure phosphorus pentachloride (Note 1). The flask is provided with an exit tube leading to the surface of a flask of water, in order to absorb the hydrogen chloride formed during the reaction. The flask is placed on a water bath and heated with occasional shaking until the reaction starts (fifteen to forty-five minutes). Vigorous evolution of hydrogen chloride takes place, and the heating is continued until the reaction is complete (fifteen to thirty minutes after the reaction starts). There is thus formed a light yellow, homogeneous liquid.

The reaction mixture is now transferred to a Claisen flask connected with a water-cooled condenser, and the phosphorus oxychloride is removed at ordinary pressure by raising the temperature of the oil bath (Note 2) gradually to 200–220°. The water condenser is then replaced by a *short* air-cooled condenser and the residual liquid is distilled under reduced pressure (Note 3). A small quantity of phosphorus oxychloride first distils over, after which the receiver is changed and the temperature rises rapidly to the boiling point of *p*-nitrobenzoyl chloride, 197°/73 mm. (155°/20 mm.). During this distillation the oil bath should be kept at a temperature of about 230–250° (or at 210–215° if 20 mm. pressure is used). The yield is 500–534 g. (90–96 per cent of the theoretical amount). The distillate

solidifies to a yellow crystalline mass melting at 71° (Note 4). The product may be recrystallized from ligroin or carbon tetrachloride, from which it separates in fine yellow needles melting at 73°.

## 2. Notes

1. The yield of *p*-nitrobenzoyl chloride depends to a great extent upon the quality of the reagents used. With impure phosphorus pentachloride and pure *p*-nitrobenzoic acid, yields of 70–80 per cent of the product are obtained. With pure phosphorus pentachloride and a less pure grade of *p*-nitrobenzoic acid, yields of 85–90 per cent are obtained. When neither reagent is of high grade, yields may fall as low as 40–50 per cent of the theoretical amount. In all such cases the color of the original reaction mixture varies from a deep yellow to a black.

Phosphorus pentachloride purchased as pure is occasionally of inferior quality and gives poor results. It is not a difficult matter to prepare in the laboratory a product suitable for this reaction. To 1000 g. of phosphorus trichloride, chlorine is added until the increase in weight is 500 g. The gas should be added above the surface of the liquid, which is stirred occasionally during the addition. The stirring should not be continuous, however, as this tends to allow the formation of the pentachloride in the tube, which thus becomes clogged. At the end of the reaction the mixture becomes practically solid.

2. If the reaction mixture is heated with a free flame during the distillation under reduced pressure, there is considerable danger of superheating and consequent decomposition (sometimes violent) of the *p*-nitrobenzoyl chloride.

Experience with many preparations of this acid chloride has shown that it is desirable to use, during the distillation under reduced pressure, a safety water-bottle between the receiving flask and the manometer. This avoids the passage of vapors of phosphorus oxychloride or acid chloride into the pump.

3. At the beginning of the distillation under reduced pressure the air condenser is warmed gently with a free flame to prevent solidification of the first portion of the distillate.

4. The product is best placed while hot in small wide-mouth bottles and allowed to solidify. This prevents any moisture from the air from decomposing more than the surface layer of the acid chloride.

### 3. Other Methods of Preparation

*p*-Nitrobenzoyl chloride has been prepared only by the action of phosphorus pentachloride on *p*-nitrobenzoic acid.[1]

[1] Ann. **221**, 335 (1883).

XXIV

## *m*-NITROCHLOROBENZENE

$$NO_2 \cdot C_6H_4 \cdot NH_2 + HCl + NaNO_2 \rightarrow NO_2 \cdot C_6H_4 \cdot N_2Cl + NaCl + 2H_2O$$

$$NO_2 \cdot C_6H_4 \cdot N_2Cl + CuCl \rightarrow NO_2 \cdot C_6H_4 \cdot Cl + N_2 + CuCl$$

Prepared by W. W. HARTMAN and M. R. BRETHEN.
Checked by C. S. MARVEL and C. R. NOLLER.

### 1. Procedure

To a solution of 1200 g. of copper sulfate and 400 g. of sodium chloride in 4 l. of water at 60–70° is added a concentrated solution of 200 g. of (90–95 per cent) sodium bisulfite (prepared if desired by saturating with sulfur dioxide a solution of 100 g. of sodium carbonate). The white precipitate of cuprous chloride is filtered off, sucked dry as rapidly as possible, and suspended in a mixture of 2 l. of water and 1500 cc. of concentrated hydrochloric acid (Note 1).

In the meantime, 552 g. of good commercial *m*-nitroaniline, melting at 110° or above (Note 2), is dissolved in a mixture of 500 cc. of hydrochloric acid and 1 l. of hot water; 1100 cc. of hydrochloric acid is then added, and the solution is cooled rapidly, with stirring. It is then surrounded with a freezing mixture, and diazotized at a temperature below 1° by adding, with constant stirring, a solution of 288 g. of technical (95 per cent) sodium nitrite in 700 cc. of water, care being taken to avoid adding an excess over that necessary to produce a distinct reaction with starch-iodide paper (cf. pp. 7–8). This point is reached when all but about 25 cc. of the nitrite solution has been added; the addition requires about an hour and a half. The cold solution is now filtered in order to remove some amorphous insoluble matter; this solid, when dry, weighs 50–55 g.

The clear filtrate, which has only a pale yellow color, is now run, with stirring, into the cuprous chloride solution in a 12-l. flask, while the temperature is kept at 25–30° (Note 3). A somewhat sticky precipitate first forms, which later becomes crystalline; nitrogen is evolved in a continuous stream. The addition requires about thirty minutes. The mixture is then warmed on a steam bath under an efficient reflux condenser until the evolution of nitrogen ceases. It is then distilled in a current of steam (using the apparatus described in Vol. II, pp. 80–82) until no more nitrochlorobenzene passes over; 9–10 l. of distillate collects during this process (Note 4). When quite cold, the water is decanted off, and the solid shaken with 1–2 l. of 1 per cent sodium hydroxide solution at 50°. The mixture is again allowed to cool, and the light yellow alkaline solution is decanted from the solid product, which is then collected on a filter, washed with a little cold water, dried, and distilled under reduced pressure. It boils completely at 116–117°/12 mm. or 124–125°/18 mm., and the distillate solidifies to 430–450 g. (68–71 per cent of the theoretical amount) of a pale yellow solid which melts at 44–45°.

## 2. Notes

1. It is more convenient to prepare cuprous chloride by reducing copper sulfate with sodium bisulfite than by the action of copper upon cupric chloride (see also p. 33). It is well to test a sample of the filtrate with sodium bisulfite solution; no further cuprous chloride should separate.

2. The yield will, of course, depend upon the quality of the nitroaniline. The pure amine would yield none of the insoluble substance on diazotization, but the cost of purification would be prohibitive. It may be noted that if the weight of the insoluble residue be deducted, the yield amounts to 75–78 per cent of the theoretical amount.

3. It is important that the temperature should be held at 25–30° during the addition of the diazonium chloride to the cuprous chloride solution. At lower temperatures the decomposition of the unstable additive compound proceeds too slowly,

and would cause too violent an evolution of nitrogen on warming; at higher temperatures the formation of tarry by-product increases.

4. If desired, the steam distillation may be omitted, since the proportion of non-volatile resinous impurities is very low. In this case the reaction mixture is allowed to cool, and the watery solution is decanted; the residue is then dissolved in 1–2 l. of benzene, and the benzene solution washed with water and with dilute alkali, after which the solvent is removed by distillation on the steam bath and the residue distilled under reduced pressure. The yield and purity of the final product are equally satisfactory.

An iron condenser should not be used in the steam distillation of the crude *m*-nitrochlorobenzene, as some reduction takes place and the yield is lowered by 10 to 15 per cent. The product is also deeply colored.

## 3. Other Methods of Preparation

*m*-Nitrochlorobenzene is not formed when chlorobenzene is nitrated, but is the chief product of the chlorination of nitrobenzene. The reaction takes place with difficulty, and it is necessary to use a catalyst, such as iodine,[1] ferric chloride [2] or antimony trichloride.[3]

The replacement of one nitro group in *m*-dinitrobenzene by a chlorine atom by means of partial reduction and diazotization has been described by Griess.[4]

[1] Ber. 7, 1765 (1874).
[2] J. prakt. Chem. (2) **36**, 25 (1887).
[3] Ann. **182**, 102 (1876).
[4] Jahresber. **1863**, 423; **1866**, 457.

XXV

# NITROMETHANE

$$Cl \cdot CH_2 \cdot CO_2Na + NaNO_2 \rightarrow NO_2 \cdot CH_2 \cdot CO_2Na + NaCl$$
$$NO_2 \cdot CH_2 \cdot CO_2Na + H_2O \rightarrow NO_2 \cdot CH_3 + NaHCO_3$$

Prepared by F. C. WHITMORE and MARION G. WHITMORE.
Checked by H. T. CLARKE and J. H. BISHOP.

## 1. Procedure

To a mixture of 500 g. of chloroacetic acid and 500 g. of cracked ice, is added, with stirring, just sufficient cold 40 per cent sodium hydroxide solution to make the solution faintly alkaline to phenolphthalein. About 360 cc. is required; the temperature should not rise above 20° (Note 1). The solution is then mixed with 365 g. of sodium nitrite dissolved in 500 cc. of water and heated in a 3-l. round-bottom flask fitted with a two-hole stopper containing a bent tube of large diameter connecting with an efficient condenser (set downward for distillation) and a thermometer dipping into the liquid. The receiver should be so arranged that it can be cooled, if necessary, by a stream of water.

The solution is heated slowly until the first appearance of bubbles of carbon dioxide, which occurs when the temperature has reached about 80°. The flame is then removed and the reaction allowed to proceed by itself (Note 2). If no rise in temperature occurs, heat is very cautiously applied until the temperature rises to 85°, when the flame is again removed. At this temperature the exothermic decomposition of the sodium nitroacetate becomes so rapid that the temperature rises almost to 100° without further application of external heat. If heat is applied after the temperature of the liquid reaches 85°, violent frothing will occur, with serious loss of nitromethane. If the

reaction becomes too vigorous it may be checked by applying a wet towel to the flask. Nitromethane starts to distil over at about 90°. During the spontaneous heating, about 120 cc. of nitromethane distils over, accompanied by about 170 cc. of water (Note 3). This water is saved for redistillation.

When the mixture ceases to maintain its temperature spontaneously at 95–100°, heat is applied cautiously until the temperature reaches 110°. About 13 cc. of nitromethane and 200 cc. of water distil over. Further distillation gives water which contains too little nitromethane to pay for recovery. At this point enough sodium chloride and sodium carbonate have separated to cause serious bumping.

The water separated from the nitromethane distillates is mixed with one-quarter of its weight of salt, and redistilled, yielding 10–12 cc. of nitromethane and about 100 cc. of water. This water on distillation gives 3–4 cc. of nitromethane and about 45 cc. of water (Note 4).

The total yield of moist product is 125–135 g.; on drying with a little calcium chloride and distilling, 115–125 g. of pure nitromethane, boiling at 98–101°, is obtained (35–38 per cent of the theoretical amount). A small forerun distils over below 98° and a little dark brown residue remains.

## 2. Notes

1. In making the sodium chloroacetate, the use of sodium hydroxide with proper cooling is much more rapid than the use of sodium carbonate. In the case of sodium hydroxide it is essential to keep the solution cool in order to prevent the formation of sodium glycollate. If it is preferred to employ sodium carbonate, about 300 g. of the anhydrous material will be required to make the solution slightly alkaline.

2. The thermometer dipping *in the liquid* is absolutely necessary, as the success of the preparation depends on proper temperature control. The vital point of the whole preparation is to remove all external heat as soon as the reaction is well started. This is between 80 and 85°. No frothing ever occurs when this precaution is rigidly adhered to.

3. It has been recommended [1] that use be made of a gravity separator connected with the adapter in order to separate the nitromethane as fast as it condenses. It was found inadvisable to use such a separator, as the nitromethane is so little heavier than water that a rapid separation is not possible; drops of nitromethane remain suspended and pass over with the water. It is best to allow the distillates to stand in cylinders for at least half an hour before separating the nitromethane by means of a separatory funnel. During this standing, as much as 2 per cent more of nitromethane sometimes settles out.

4. If the time consumed is an important consideration, it is well to note that the spontaneous heating from 85 to 100° gives three-quarters of all the nitromethane obtained in the preparation. This takes less than one hour. The further heating above 100° and the distillations of the water layers take over two hours, and give only one-quarter of the total yield.

5. Several of these distilling sets can be set up and run by one operator, if each lot is started only when the preceding one has reached 85° and external heat has been removed. The corresponding water layers from different sets can be united and distilled at once.

## 3. Other Methods of Preparation

Nitromethane has been prepared by the action of methyl iodide on silver nitrite; [2] by the action of methyl sulfate on potassium nitrite; [3] by the oxidation of methylamine by Caro's reagent; [4] by the interaction of potassium nitrite and potassium chloroacetate,[5] or, preferably,[1] the corresponding sodium salts.[6] The use of the calcium salts was found to be of no advantage.[1] The only one of the above methods to be studied was the interaction of the sodium salts in boiling aqueous solution.

[1] Ber. **42**, 3438 (1909).
[2] Ann. **171**, 32 (1874).
[3] Ber. **40**, 3216 (1907).
[4] Ber. **35**, 4300 (1902).
[5] J. prakt. Chem. (2) **5**, 427 (1872); (2) **8**, 316 (1874); Ber. **41**, 4457 (1908).
[6] Bull. soc. chim. (3) **23**, 333 (1900); (4) **5**, 180 (1909).

## XXVI

### *m*-NITROPHENOL

$$NO_2 \cdot C_6H_4 \cdot NH_2 + H_2SO_4 + HNO_2 \rightarrow NO_2 \cdot C_6H_4 \cdot N_2 \cdot OSO_3H$$
$$NO_2 \cdot C_6H_4 \cdot N_2 \cdot OSO_3H + H_2O \rightarrow NO_2 \cdot C_6H_4 \cdot OH + N_2 + H_2SO_4$$

Prepared by Roger Adams and W. C. Wilson.
Checked by Oliver Kamm and A. O. Matthews.

### 1. Procedure

In a 500-cc. round-bottom flask are placed 200 cc. of water, 100 cc. of concentrated sulfuric acid, and 50 g. of powdered *m*-nitroaniline. The hot mixture is shaken until solution is complete, and the hot *m*-nitroaniline sulfate solution is then poured into a 5-l. flask containing 1000 cc. of water and 800–1000 g. of cracked ice. During this procedure there must be good agitation, so that the *m*-nitroaniline sulfate forms a finely divided precipitate. Generally, the amount of ice used is sufficient to lower the temperature of the mixture to 0°, but if not, more ice is added till 0° is reached.

A solution of 26 g. of sodium nitrite in 200 cc. of water is then rapidly added (Note 1) to the cold *m*-nitroaniline sulfate suspension; continual shaking or mechanical stirring should be used until the *m*-nitroaniline sulfate dissolves completely. This requires about five minutes, during which period the solution gradually darkens. A small flocculent precipitate forms at the same time and should be filtered off.

A mixture of 6 l. of water and 600 cc. of concentrated sulfuric acid is placed in a 12-l. round-bottom flask, and to it the diazonium salt solution is added all at once; the resulting mixture is then heated to boiling as rapidly as possible. The solution becomes turbid at first but gradually becomes clear after boiling for about forty minutes. The solution, which now contains a

small amount of tarry material, is filtered with suction through a Buchner funnel provided with 2–3 cm. of sand on top of the filter paper.

The filtered solution is now cooled, which causes a small amount of *m*-nitrophenol to separate. This is not filtered off, but the whole solution is extracted with ether (750–1000 cc. in

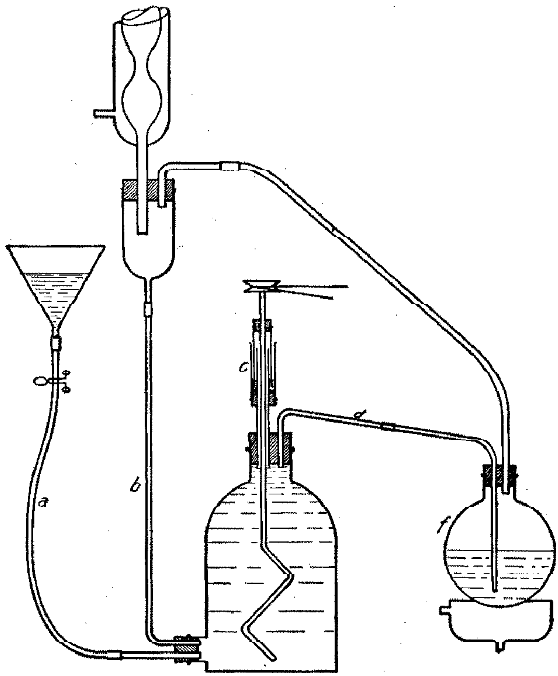



FIG. 3.

the flask and 500–750 cc. in the bottle) in the continuous extractor shown in the accompanying diagram and described in Note 3. About two hours' time is necessary. The ether is distilled off, and the remaining oil, when cooled, solidifies to yellow crystals of crude *m*-nitrophenol. The crystals are transferred to a beaker and washed with a small quantity of cold benzene, to take out most of the yellow color which is present. The yield of this partially purified product amounts to 40–43 g. (80–85 per cent

of the theoretical amount). The cream-colored product thus obtained melts at 90° and is satisfactory for most purposes but may be purified as follows: the *m*-nitrophenol is dissolved in hot hydrochloric acid (1 part of concentrated hydrochloric acid to 1 part of water, by volume), filtered and cooled to 0°, when light yellow crystals separate. An alternative method is to distil under reduced pressure (b. p. 182–189°/12 mm.) and recrystallize the distillate from benzene; in this way a product which melts at 96° is obtained.

## 2. Notes

1. In diazotizing *m*-nitroaniline sulfate, it is necessary to add the sodium nitrite as rapidly as possible in order to prevent any of the diazonium salt from coupling with undiazotized *m*-nitroaniline and forming a yellow precipitate of diazoamino compound. The presence of the excess of sulfuric acid, which does not interfere with the formation of the *m*-nitrophenol, tends to avoid this same difficulty.

2. The hydrolysis of the diazonium salt must be carried out in a dilute solution. A higher concentration greatly increases the amount of tar formed and diminishes the yield of *m*-nitrophenol. Moreover, the amount of tar formed is less, provided the solution of diazonium salt and dilute sulfuric acid is raised to the boiling point as rapidly as possible.

3. The apparatus shown (Fig. 3) is a very convenient form of continuous extractor for the laboratory. In the flask *f* is placed two-thirds of the solvent to be used for the extraction. The remainder is placed in the bottle, which should be just large enough to accommodate the solution to be extracted and the rest of the solvent. The flask is heated on a bath, causing the vapors to pass through *e* into the condenser, and the liquid therefrom flows through *b* into the bottom of the bottle, the contents of which must be mechanically stirred during the extraction in order to obtain efficient contact of the liquids. The stirrer and mercury seal are represented by *c*. For emptying and filling the bottle without disconnecting the apparatus,

the tube *a* with pinchcock is provided. The only precaution to be mentioned is that occasionally the solution in the flask *f* becomes too concentrated, and consequently so hot that the ether cannot flow back through *d* owing to its rapid vaporization. If this happens, the contents of the flask must be removed and replaced by fresh solvent.

There is no value in adding salt to the solution before extraction.

The ether recovered amounts to 1000–1100 cc.

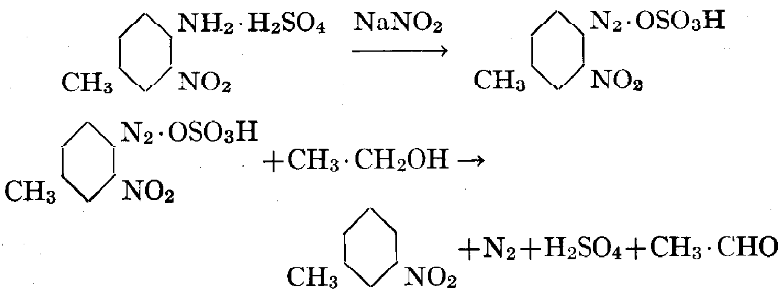
### 3. Other Methods of Preparation

*m*-Nitrophenol has been made by diazotizing *m*-nitroaniline and subsequently heating with a large volume of water.

[1] Ber. **7**, 179 (1874); Ann. **215**, 323 (1882); Rec. trav. chim. **2**, 216 (1883).

# XXVII

## *m*-NITROTOLUENE




Prepared by H. T. CLARKE and E. R. TAYLOR.
Checked by J. B. CONANT and L. F. LEA.

### 1. Procedure

To 500 g. of 95 per cent ethyl alcohol in a 5-l. flask are added 170 g. of "*m*-nitro-*p*-toluidine" (3-nitro-4-aminotoluene, m. p. 112–114°, Note 1) and 250 g. of concentrated sulfuric acid. The solution is chilled to 10° by means of an ice bath, and a solution of 85 g. of technical sodium nitrite in a minimum quantity of water is slowly added, with stirring, the temperature being kept below 10°. The mixture is now warmed very gently on the water bath under an efficient reflux condenser (from the upper end of which a tube leads to a hood or through water) until evolution of gas ceases (Note 2). The alcohol and aldehyde are then carefully distilled off, using a fractionating column and heating in an oil or brine bath (Note 3); when the temperature of the vapors reaches 80° fractionation is stopped and the residue is distilled in a current of steam. The oil is separated from the distillate and the aqueous portion shaken out once with 150–200 cc. of benzene. The united oil and extract are dried with a

small quantity of calcium chloride and distilled, first under normal pressure to remove the benzene, and finally under reduced pressure. The *m*-nitrotoluene passes over entirely at 113–114°/15 mm. On cooling it forms a pale yellow solid which melts at 16°. The yield of pure material is 95–110 g. (67–77 per cent of the theoretical amount).

## 2. Notes

1. "*m*-Nitro-*p*-toluidine" of good quality is readily available, since it is employed as an intermediate in the preparation of certain important pigments.

2. The decomposition of the diazonium sulfate in the presence of alcohol may take place with considerable violence, and it is necessary to watch the reaction carefully so as to be able to check it, if necessary, by the external application of cold water. Acetaldehyde is rapidly evolved, and some will generally escape from the condenser. It is therefore advisable to lead the escaping gases through water, not only in order to avoid possibility of fire, but to retain any nitrotoluene which may be entrained.

3. If after the reaction the alcohol be distilled off without the use of a column it will contain an appreciable quantity of *m*-nitrotoluene, amounting to 5 or more per cent of the yield. The use of an oil or brine bath is recommended on account of the presence of solid inorganic salts in the mixture.

## 3. Other Methods of Preparation

*m*-Nitrotoluene is formed in very small amount during the nitration of toluene; its presence was first proved by the isolation of *m*-nitrobenzoic acid from the mixture of acids produced on oxidation.[1] It has actually been isolated in a nearly pure condition from the oily by-product obtained in the manufacture of dinitrotoluene, by taking advantage of the fact that it is much less easily nitrated than either the ortho or the para isomer.[2]

[1] Ber. **12**, 443 (1879).
[2] Ber. **18**, 1336 (1885).

The method of preparation adopted is substantially that of Buchka,[3] as this is the only one of practical value. *m*-Nitrotoluene has been obtained by a similar process from 5-nitro-2-aminotoluene [4] (obtained by nitration of acetyl-*o*-toluidine), but this compound is not commercially available, and gives a poor product unless carefully purified.

[3] Ber. **22**, 829 (1889); *cf.* J. Amer. Chem. Soc. **41**, 1565 (1919).
[4] Ann. **158**, 348 (1871).

# XXVIII

## PHENYLUREA

*(by-product, Carbanilide)*

$$C_6H_5 \cdot NH_2 \cdot HCl + CO(NH_2)_2 \rightarrow C_6H_5 \cdot NH \cdot CO \cdot NH_2 + NH_4Cl$$

$$C_6H_5 \cdot NH_2 \cdot HCl + C_6H_5 \cdot NH \cdot CO \cdot NH_2 \rightarrow (C_6H_5 \cdot NH)_2CO + NH_4Cl$$

Prepared by TENNEY L. DAVIS and K. C. BLANCHARD.
Checked by C. S. MARVEL and W. B. KING.

### 1. Procedure

A SOLUTION of 390 g. of aniline hydrochloride (3 mols) and 190 g. of urea (3.16 mols) in 1500 cc. of water is boiled in a 3-l. flask under a reflux condenser (Note 2). After about one hour, crystals begin to separate; at the end of one and a half to two hours, the mixture, which bumps considerably, is cooled, filtered by suction, and the crystals of carbanilide washed with 100 cc. of boiling water. The filtrate is chilled and the phenylurea which crystallizes out is filtered off and rinsed with a little cold water, the washings being discarded. The filtrate is again boiled under a reflux condenser for one and a half to two hours, or until it begins to bump, and the process is repeated. The above operations are gone through still a third time, and each time the phenylurea is collected from the cold filtrate. The mother liquor is finally evaporated to half its original volume and additional crops of carbanilide and phenylurea are so obtained. Further evaporation is not profitable.

The crude carbanilide (symmetrical diphenylurea) is practically pure, and may be obtained in large colorless needles melting at 235° by recrystallization from alcohol with the use of decolorizing carbon; 1 l. of alcohol is required for every 25 g. of

product (Note 3). The weight of the crude carbanilide is 122–128 g. (38–40 per cent of the theoretical amount).

The crude phenylurea is somewhat colored and contains a little carbanilide. It may be purified by dissolving in a minimum quantity of boiling water, adding a little decolorizing carbon, and filtering. When the filtrate first begins to cool, a flocculent precipitate of carbanilide is deposited; this must be filtered off while the liquid is still hot. The filtrate, on cooling, yields colorless stout needles or flakes of phenylurea melting at 147° (Note 4). The total weight of pure product is 212–225 g. (52–55 per cent of the theoretical amount).

## 2. Notes

1. The reaction can undoubtedly be explained by the formation of an equilibrium mixture of urea and ammonium cyanate in boiling solution; the ammonium cyanate reacts at the moment of its formation with aniline hydrochloride, yielding phenylurea. This latter compound also undergoes a secondary reaction, involving the intermediate formation of phenyl isocyanate, which reacts with aniline hydrochloride forming carbanilide; so that in order to obtain the best yield it is necessary to interrupt the process from time to time and remove the phenylurea first formed.

That the reaction proceeds to completion under the above conditions is shown by the fact that while the mixture ultimately becomes faintly alkaline (on account of the formation of ammonia by hydrolysis of the excess of urea) at no time does the mixture appear to contain aniline.

2. In the above directions the concentration is as high as it is safe to make it; if less water be used the yield of phenylurea decreases and there is grave danger of loss due to the sudden heating of the mixture by rapid separation of crystals. This phenomenon has been observed with a more concentrated mixture even on heating on the steam bath.

3. The carbanilide can also be obtained in long needles from glacial acetic acid or preferably ethyl acetate.

4. If the solution of phenylurea be allowed to cool slowly, the product separates in needles several centimeters in length.

### 3. Other Methods of Preparation

Of the various published methods of preparing phenylurea, such as treatment of aniline salts with potassium cyanate in water solution,[1] heating aniline with urea,[2] with cyanic acid,[3] or with cyanogen chloride,[4] and the interaction of phenyl isocyanate or phenylcarbamine chloride with ammonia,[5] the only ones to be considered as practical methods for preparation are the first two. The first suffers from the disadvantage that potassium cyanate is not easily prepared in the laboratory and rapidly undergoes spontaneous decomposition in storage; while by the action of urea on aniline alone, carbanilide is formed in rather larger proportion than phenylurea.

While the preparation of phenylurea itself by the foregoing process does not appear in the older literature, an analogous process has been patented for the preparation of *p*-phenetylurea,[6] in which *p*-phenetidine is heated with urea nitrate (or *p*-phenetidine hydrochloride with urea) in aqueous solution. This reaction appears to be generally applicable to aromatic primary amines; it does not, however, appear to be so well suited to the preparation of the corresponding derivatives of secondary amines.

[1] Ann. **57**, 265 (1846); Ber. **9**, 820 (1876).
[2] Ber. **9**, 995 (1876); J. Am. Chem. Soc. **44**, 2600 (1922).
[3] J. Chem. Soc. **77**, 33 (1900).
[4] Ann. **70**, 130 (1849).
[5] Ann. **74**, 13 (1850); Am. Chem. J. **16**, 72 (1894).
[6] D. R. P. 76,596, Frdl. **4**, 1268 (1894–97).

# XXIX

## *p*-TOLYLMERCURIC CHLORIDE

$$CH_3 \cdot C_6H_4 \cdot SO_2Na \cdot 2H_2O + HgCl_2 \rightarrow CH_3 \cdot C_6H_4 \cdot HgCl + NaCl + SO_2 + 2H_2O$$

Prepared by F. C. Whitmore, Frances H. Hamilton and N. Thurman.
Checked by J. B. Conant and F. C. Whidden.

### 1. Procedure

To 1 l. of boiling water in a 3-l. beaker or large evaporating dish (Note 1) is added 150 g. of mercuric chloride; to this mixture is then added, with good stirring, 116 g. of sodium *p*-toluenesulfinate (Vol. II, p. 89). A thick, white, curdy precipitate forms at once (Note 2), and in a short time sulfur dioxide is evolved copiously. The heating and stirring are continued until no more sulfur dioxide is evolved, which requires about two hours.

The mixture is then filtered by suction, and the precipitate dried in an oven at about 80° for twelve hours. The dry precipitate is then placed in a 1-l. round-bottom flask with reflux condenser, and covered with 800 cc. of xylene. The mixture is agitated by shaking, the xylene heated to boiling for five to ten minutes, and the solution filtered through a hot funnel to remove the calomel which is formed during the reaction. The filtrate is cooled, the *p*-tolylmercuric chloride filtered off, and the first precipitate extracted again with the filtrate. This is repeated twice. In this way 90–100 g. (51–57 per cent of the theoretical amount) of a product which melts at 233° is obtained.

## 2. Notes

1. It is essential that the vessel employed should be of at least 3 l. capacity. If it be smaller, the contents will probably overflow during the first evolution of sulfur dioxide.

2. A large amount of calomel is formed in this reaction owing to the reduction of the mercuric chloride by the sulfurous acid formed. This reduction produces hydrochloric acid which probably changes some of the mercury compound to toluene and mercuric chloride. An attempt was made to avoid this action by adding sodium hydroxide slowly during the process to keep the solution from becoming strongly acid, but the yield was increased only slightly. The yield was not increased by adding the sulfinate to the mercuric chloride gradually or by reversing this process.

3. There is always a considerable amount of inorganic mercury left in the filtrate, which gives very little more of the tolylmercuric chloride when treated with more of the sulfinate. This may be present largely in the form of the mercuric salt of *p*-toluenesulfonic acid produced by the oxidation of some of the sulfinic acid liberated in a side-reaction.

## 3. Other Methods of Preparation

*p*-Tolylmercuric chloride has been prepared from *p*-toluenesulfinic acid and mercuric chloride,[1] from *p*-toluenesulfochloride and mercury diphenyl at 120°,[2] by treating *p*-tolueneboric acid with mercuric chloride,[3] by the direct mercuration of toluene with mercuric acetate,[4] from *p*-tolylmercuric nitrate and hydrochloric acid,[5] from hydrochloric acid and *p*-tolylmercuric hydroxide formed by the oxidation of mercury di-*p*-tolyl,[6] and from mercury di-*p*-tolyl by heating with mercuric chloride in alcohol.[7]

[1] Ber. **38**, 2569 (1905).
[2] Ber. **18**, 249 (1885).
[3] Ber. **15**, 185 (1882).
[4] Ber. **32**, 761 (1899); *cf.* Ann. **413**, 329 (1917).
[5] Ber. **31**, 1528 (1898).
[6] J. prakt. Chem. (2) **29**, 138 (1884).
[7] J. prakt. Chem. (2) **1**, 185 (1870).

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# ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS




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# PREFACE TO VOLUME IV

The general plan outlined in the first volume of the series has been followed in the subsequent publications; but it has been found advisable to include preparations which are carried out on a somewhat reduced scale, since the carefully described directions have found application not merely in the semi-commercial preparation of needed research chemicals and reagents but also in the instruction of graduate students entering the organic field. However, it is the experience of the editors that the reduction of preparations described on a large scale is usually less difficult than the reverse procedure.

The sections on "Other Methods of Preparation" are not intended to include all possible methods but rather those that are of interest chiefly from the preparative standpoint. The Cumulative Index, started with Volume III, is being continued.

The friendly cooperation of other workers in Organic Chemistry has been gratifying, and the editors again cordially invite contributions from any investigator who has occasion to study an organic preparation exhaustively enough to justify the presentation of certified directions.

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# ORGANIC SYNTHESES

## I

## ACETYL MANDELYL CHLORIDE

$$C_6H_5CHOHCO_2H + CH_3COCl \rightarrow C_6H_5CH(OCOCH_3)CO_2H + HCl$$

$$C_6H_5CH(OCOCH_3)CO_2H + SOCl_2 \rightarrow C_6H_5CH(OCOCH_3)COCl + SO_2 + HCl$$

Prepared by F. K. THAYER.
Checked by ROGER ADAMS and E. E. DREGER.

### 1. Procedure

IN a 500-cc. Claisen distilling flask with a low side-tube connected to a condenser, are placed 105 g. of mandelic acid (m.p. 118°) and 151 g. of acetyl chloride. A reaction sets in without the application of heat (Note 1). As soon as a clear solution results, the flask is warmed on a water bath and the excess acetyl chloride is distilled. The last trace of acetyl chloride may be removed by prolonged drying in a vacuum. The acetyl mandelic acid then crystallizes in large, round, white clusters after one or two days' standing. The yield is 130–133 g. (97–99 per cent of the theoretical amount) (Note 2).

To the crude acetyl mandelic acid still containing some acetyl chloride obtained as described above, is added 250 g. of thionyl chloride. The reaction starts at once without warming but it is necessary to reflux for four hours to complete the reaction (Note 3). The excess thionyl chloride is then distilled

and the residue distilled in a vacuum (Note 4). The yield is 115–120 g. (79–83 per cent of the theoretical amount) of almost colorless liquid boiling at 125–130°/10 mm. (150–155°/33 mm.).

## 2. Notes

1. Occasionally the application of a little heat is necessary to bring about a more rapid acetylation.

2. The melting points given in the literature range from 39 to 80°. The acetyl mandelic acid is difficult to crystallize but may be purified from benzene or chloroform, preferably the former. The product thus obtained melts at about 79–80°.

3. Prolonged refluxing of the acetylated mandelic acid with the thionyl chloride tends to lower the yield.

4. Anschütz gives the boiling point of acetyl mandelyl chloride as 129°/10 mm. The vacuum used should be as low as possible, to avoid the formation of tar during the distillation.

## 3. Other Methods of Preparation

Acetyl mandelic acid was described by Naquet and Louguinine,[1] but their product has been shown to be contaminated with the ethyl ester of acetyl mandelic acid. Dupont[2] obtained the compound by the oxidation of diacetyl 1, 4-diphenylbutine-2-diol-1, 4. Anschütz and Böcker[3] prepared acetyl mandelic acid, and from it the acid chloride, by the use of phosphorus pentachloride, but with poor yields. Von Braun and Müller[4] state that acetyl mandelyl chloride can be made from acetylated mandelic acid and thionyl chloride, the resulting product being a viscous yellow oil.

[1] Compt. rend. **62**, 430 (1866); Ann. **139**, 302 (1866).
[2] Compt. rend. **150**, 1525 (1910).
[3] Ann. **368**, 57, 59 (1909).
[4] Ber. **51**, 244 (1918).

# α-AMINO-n-CAPROIC ACID

$$CH_3(CH_2)_3CHBrCO_2H + 2NH_3 \rightarrow CH_3(CH_2)_3CHNH_2CO_2H + NH_4Br$$

Prepared by C. S. MARVEL and V. DU VIGNEAUD.
Checked by H. T. CLARKE and E. R. TAYLOR.

## 1. Procedure

IN a 1-l. round-bottom flask is placed 760 g. of concentrated ammonium hydroxide (sp. gr. 0.9) and to this is slowly added 150 g. of α-bromocaproic acid (Note 1). The flask is well stoppered and allowed to stand in a warm place (50–55°) for twenty to thirty hours. The amino acid separates and is filtered off with suction and washed with methyl alcohol (Note 2). This crop of crystals weighs 51–56 g. The aqueous filtrate is evaporated nearly to dryness on a steam bath and then treated with about 250 cc. of methyl alcohol. This precipitates a second crop of amino acid contaminated with ammonium bromide. On washing with methyl alcohol and recrystallizing from water, there is obtained 10–15 g. more of pure product. The total yield is 63–68 g. (62–67 per cent of the theoretical amount).

## 2. Notes

1. The once-distilled bromocaproic acid (p. 9) is satisfactory.

2. If the amino acid is not carefully washed with alcohol, it contains ammonium bromide and may possess an objectionable

odor. Methyl alcohol is preferable to ethyl alcohol since it dissolves ammonium bromide more readily.

## 3. Other Methods of Preparation

*α*-Amino-*n*-caproic acid has been prepared by the action of ammonia on *α*-bromo-*n*-caproic acid.[1]

[1] J. prakt. Chem. (2) **1**, 7 (1870); Ber. **33**, 2381 (1900); Z. physiol. Chem. **86**, 456 (1913); J. Am. Chem. Soc. **42**, 320 (1920).

## III

# ARSONO- AND ARSENOACETIC ACIDS

$$ClCH_2CO_2Na + Na_3AsO_3 \rightarrow NaCl + CH_2(CO_2Na)AsO_3Na_2$$

$$2CH_2(CO_2H)AsO_3H_2 + 8H(H_3PO_2) \rightarrow \begin{array}{l} AsCH_2CO_2H + 6H_2O \\ \| \\ AsCH_2CO_2H \end{array}$$

Prepared by C. S. Palmer.
Checked by Oliver Kamm.

## 1. Procedure

One hundred grams of powdered arsenious oxide is added to the hot solution obtained by dissolving 160 g. of sodium hydroxide in 300 cc. of water. After the solution has cooled to 20°, 48 g. of chloroacetic acid is added. The suspension is well stirred during about five minutes, when a strongly exothermic reaction begins, the temperature rises to 70–75°, and a clear solution results.

The reaction mixture is permitted to stand at room temperature during one hour, or longer if desired (Note 1). The solution is acidified with 160 cc. of glacial acetic acid and, after the temperature has been lowered to 40° by cooling, the precipitated arsenious oxide is filtered off by suction and washed with 50 cc. of water.

The filtrate is poured into a solution containing 185 g. of crystallized barium chloride dissolved in 600 cc. of hot water. Barium arsonoacetate, $Ba(O_2CCH_2AsO_3Ba)_2$ (hydrated), forms a thick, finely divided precipitate. The mixture is stirred for several minutes and then allowed to stand until the following day, when it is filtered upon a 15-cm. Büchner funnel and washed

thoroughly with water (Note 2). The yield of air-dry * product is 220 g. (96 per cent of the theoretical amount).

Sodium arsonoacetate is prepared by adding the freshly filtered and washed barium arsonoacetate as obtained above (without drying) to a solution of 108 g. of anhydrous sodium sulfate in 500 cc. of hot water. The mixture is mechanically stirred for one hour, the barium sulfate filtered off, and the filtrate concentrated on the steam bath until crystallization commences. Upon cooling and stirring (Note 3), sodium arsonoacetate separates and is filtered by suction, the filtrate being concentrated to obtain a second crop of crystals. The yield of the combined fractions is 100–110 g. (80–88 per cent of the theoretical amount).

A solution of 12.5 g. of sodium arsonoacetate and 30 g. of sodium hypophosphite ($NaH_2PO_2 \cdot H_2O$) in 150 cc. of cold 15 per cent sulfuric acid is allowed to stand at room temperature. After two or three days, the yellow precipitate is filtered off, washed with water, and dried in a vacuum over sulfuric acid or phosphorus pentoxide. A second crop is obtained by allowing the mother liquid to stand for two days longer.

The arsenoacetic acid consists of minute yellow needles, which do not melt below 260° although they undergo considerable decomposition above 200°. The yield is 5 g. (74 per cent of the theoretical amount).

## 2. Notes

1. The reaction between sodium arsenite and chloroacetic acid is very rapid, as may easily be demonstrated by titrating 1-cc. portions of the solution with N/10 iodine, according to the usual volumetric method for arsenious acid, before and after the reaction with chloroacetic acid. The excess of sodium arsenite is necessary, as was learned by means of an iodometric study of the reaction.

* The air-dry sample contains 13 per cent of water of hydration, as determined by actual analysis.

2. If the thick paste is not allowed to stand over night, filtration is more cumbersome and it is extremely difficult to wash the precipitate free from arsenites. With this precaution, it is found that after five washings with 250-cc. portions of water, the final filtrate, as well as the desired barium salt, is practically free from iodine-reducing compounds.

3. Stirring is required during the crystallization process, since otherwise the product tends to form a solid cake. The sodium salt is obtained without water of crystallization. Usually, it contains a trace of sulfate but this does not interfere with its subsequent use. The sulfate may be removed by recrystallization from water.

## 3. Other Methods of Preparation

Arsonoacetic acid was obtained by Ehrlich and Bertheim [1] by treating *p*-aminophenylarsenoacetic acid with bromine. It has been prepared by the action of three molecular equivalents of sodium chloroacetate on two of sodium arsenite, followed by isolation as the calcium salt,[2] but it is found that these proportions are less satisfactory than the ones adopted.[3] Arsenoacetic acid has been prepared recently by Palmer.[3]

[1] Ber. **43**, 926 (1910).
[2] U. S. Pat. 1,445,685; Austrian Pat. 93,325; Swiss Pat. 97,977.
[3] J. Am. Chem. Soc. **45**, 3023 (1923).

## α-BROMO-*n*-CAPROIC ACID

$$CH_3(CH_2)_4CO_2H + Br_2(PCl_3) \rightarrow CH_3(CH_2)_3CHBrCO_2H + HBr$$

Prepared by H. T. Clarke and E. R. Taylor.
Checked by C. S. Marvel and R. L. Shriner.

### 1. Procedure

Two hundred grams of freshly distilled dry *n*-caproic acid is placed in a 1-l. flask with 300 g. of bromine which has been dried by washing once with 200 cc. of concentrated sulfuric acid (Note 1). A 3-cc. portion of phosphorus trichloride is cautiously added and the flask connected to a reflux condenser (Note 2), the top of which is connected with a trap and absorption bottle containing water. The mixture is then heated in a water or oil bath to 65–70°, at which temperature the reaction commences and hydrobromic acid is given off smoothly. After five to six hours, the bromine has all reacted (Note 3). Towards the end of the reaction, the temperature is allowed to rise to about 100°. The contents of the flask are now distilled under diminished pressure (Note 4). The fraction boiling at 132–140°/15 mm. is collected and amounts to 280–298 g. (81–89 per cent of the theoretical amount).

### 2. Notes

1. The reagents must be dry or the yield will be lowered.

2. A flask fitted with a ground-glass connection to the reflux condenser will assist in reducing the amount of tar.

3. For larger runs, a longer time is required. A run of 2 kg. of caproic acid requires about fifteen hours.

4. It is best to distil the first low-boiling fractions with a water pump, since a considerable amount of hydrogen bromide is evolved. In order to obtain a light-colored product, the distillation should take place under as low pressure as possible. The $\alpha$-bromo-$n$-caproic acid boils at 116–125°/8 mm. The product obtained is sufficiently pure for most purposes; upon redistillation, however, it comes over almost entirely between 128–131°/10 mm.

## 3. Other Methods of Preparation

$\alpha$-Bromo-$n$-caproic acid has been prepared by heating $n$-caproic acid with bromine in a sealed tube to 140° [1] and with bromine and phosphorus; [2] also by the action of heat on $\alpha$-bromobutylmalonic acid.[3]

[1] Z. Chem. **1868**, 616; J. prakt. Chem. (2) **1**, 7 (1870).
[2] Ber. **24**, 2222 (1891); **33**, 2381 (1900); Z. physiol. Chem. **86**, 455 (1913).
[3] J. Am. Chem. Soc. **42**, 319 (1920).

V

## n-BUTYLMALONIC ESTER (ETHYL)

$$C_4H_9Br + CH_2(CO_2C_2H_5)_2 + C_2H_5ONa \rightarrow C_4H_9CH(CO_2C_2H_5)_2 + NaBr + C_2H_5OH$$

Prepared by ROGER ADAMS and R. M. KAMM.
Checked by F. C. WHITMORE and MILTON PUTERBAUGH.

### 1. Procedure

A 5-l. round-bottom flask, fitted with a rubber stopper holding a reflux condenser, a separatory funnel, and a mechanical stirrer, is clamped over a steam or water bath. In the flask is placed 2.5 l. of absolute alcohol (Note 1) and then there is added gradually, through the condenser, 115 g. of clean sodium cut into pieces of suitable size. If the action becomes too violent, the mixture may be cooled by water poured over the outside of the flask. The sodium alcoholate solution is stirred, and cooled to about 50°, after which 825 g. (780 cc.) of diethyl malonate (Note 2) is added slowly through the separatory funnel. To the clear solution is added gradually 685 g. (545 cc.) of *n*-butyl bromide (Note 3). The reaction commences almost immediately and considerable heat is generated. If the addition is too rapid, the reaction may become violent enough to require cooling of the flask by pouring water over it. Up to this point, the time required is about two hours.

The reaction mixture is refluxed until neutral to moist litmus; this requires about two hours. The flask is then connected with a condenser set for distillation. As much alcohol as possible is distilled off by means of the steam or water bath.

A period of about six hours is required for this distillation and about 2 l. of alcohol is recovered.

The residue from which no more alcohol can be distilled is treated with about 2 l. of water and shaken thoroughly. The upper layer of *n*-butylmalonic ester is separated (Note 4) and distilled under diminished pressure from a 2- or a 3-l. Claisen flask. First a low-boiling portion is collected, consisting of alcohol, water, and butyl bromide; then a small intermediate fraction of unchanged malonic ester comes over; and finally *n*-butylmalonic ester boiling at 140–145°/40 mm., 130–135°/20 mm., and 235–240°/760 mm. The first fractions amount to less than 100 cc., while the main fraction amounts to 860–970 g. (80–90 per cent of the theoretical amount).

## 2. Notes

1. The quality of the absolute alcohol used has a very marked effect upon the yield. It is a wise procedure to reflux ordinary "absolute" alcohol with about one-twentieth of its weight of sodium and then to distil it directly into the flask in which it is to be used.

A trial run with alcohol of 98.4 per cent purity gave only a 66 per cent yield.

2. The malonic ester used should be redistilled, preferably under diminished pressure, and a 2-degree fraction used in the preparation. Ordinary commercial malonic ester contains up to 15 per cent of low-boiling impurities.

3. Redistilled *n*-butyl bromide boiling over a 1-degree range should be used.

4. It is not practical to filter off the sodium bromide either before or after the distillation of the alcohol, as the separation of the ester from the water layer is then very difficult.

## 3. Other Methods of Preparation

*n*-Butylmalonic ester has been prepared only by the action of *n*-butyl halides on sodium malonic ester.[1]

[1] Ber. **28**, 2622 (1895); J. Am. Chem. Soc. **42**, 316 (1920).

# VI

## o-CHLOROMERCURIPHENOL

$$C_6H_5OH + Hg(OCOCH_3)_2 \rightarrow CH_3CO_2H + HOC_6H_4HgOCOCH_3$$

$$HOC_6H_4HgOCOCH_3 + NaCl \rightarrow CH_3CO_2Na + HOC_6H_4HgCl$$

Prepared by F. C. WHITMORE and E. R. HANSON.
Checked by J. B. CONANT and R. M. GRANARA.

### 1. Procedure

Two liters of water is heated to boiling in a 3-l. flask. Meanwhile 50 g. of phenol, in a 250-cc. tall beaker provided with a small glass mechanical stirrer, is heated to 170° on an electric heater (Note 1). The heat is then turned off and 100 g. of powdered mercuric acetate is added gradually (five to ten minutes) to the stirred phenol. After all of the mercuric acetate has dissolved in the phenol, the mercuration mixture is poured slowly into the hot water, the burner having previously been removed (Note 2). The beaker is rinsed out with some of the hot water. The mixture is boiled for five minutes and then filtered through filter paper in a large Büchner funnel which has been previously heated by blowing steam through it. The pink residue (Note 3) consists of a small amount of dimercurated phenol and some polymerization products.

The filtrate is again brought to boiling in a clean flask and treated with a solution of 20 g. of sodium chloride in 200 cc. of boiling water. The precipitate formed is *p*-chloromercuriphenol together with some colored impurities (Note 4). The mixture is heated to boiling and filtered through a large preheated Büchner funnel. The filtrate on cooling deposits white feathery crystals of *o*-chloromercuriphenol. The mixture is

allowed to stand at least twelve hours and then filtered. The crystals are air-dried. They should be colorless and should melt above 147° (m.p. of pure substance 152°). If the product is pink or melts low it should be recrystallized from hot water. The average yield of fifteen experiments was 45 g. of ortho compound melting above 147°, which corresponds to 44 per cent of the theoretical amount.

## 2. Notes

1. Mercuration at lower temperatures than that recommended gives a poorer yield of the ortho compound.

2. If the heat is not removed from under the water before the mercurated phenol is added, the mixture is likely to froth over.

3. Long heating of the mercuration mixture increases the amount of pink by-product.

4. The yield of impure para compound obtained as a by-product varies from 10 to 30 g.

5. A saturated solution of bromine in glycerol should be kept at hand as an antidote for phenol burns. If all undissolved bromine is allowed to settle out before the solution is used, there is no danger of bromine burns.

## 3. Other Methods of Preparation

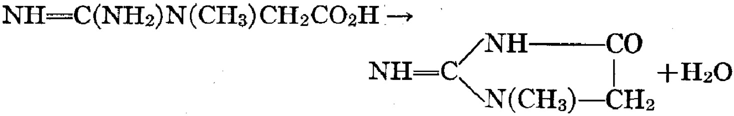
Phenol has been mercurated in water solution [1] and without the use of any solvent but the phenol itself.[2]

[1] Ber. **35**, 2855 (1902).

[2] J. Am. Chem. Soc. **43**, 622 (1921).

VII

## CREATININE



Prepared by GRAHAM EDGAR and W. S. HINEGARDNER.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

A. *Creatinine.* A mixture of 900 g. of commercial creatine hydrate (Note 1) with 550 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 150 cc. of water is warmed in a 3-l. flask on the steam bath for twenty-four hours. The hot solution is filtered and chilled to 0–5° in an ice bath, and to it is added 1000 cc. of 28 per cent aqueous ammonia (sp. gr. 0.90). The flask is immersed in an ice-salt bath and the mixture is stirred vigorously until the temperature falls to 0°, when the crystalline creatinine is filtered off, washed with ice-cold 28 per cent aqueous ammonia (Note 2) until the filtrate is free of chlorides, and finally with ice-cold methyl alcohol; the product (Note 3) is then dried to constant weight at 40–50°. The yield (Note 4) is 545–555 g. (80–81 per cent of the theoretical amount).

B. *Creatinine Zinc Chloride.* An intimate mixture of 400 g. of commercial creatine hydrate and 400 g. of fused zinc chloride is heated in a porcelain dish over a small flame. The mixture melts to a viscous liquid which soon solidifies. The flame is removed when the mixture can no longer be stirred. The mass, when cold, is broken up, and stirred with 500 cc. of cold water until the lumps are softened; the crude creatinine zinc chloride is filtered off with suction, by the use of a hardened filter paper,

and washed with ice water to remove excess zinc chloride. The crude material is now dissolved in 6 l. of boiling 25 per cent aqueous acetic acid, filtered with the use of a little decolorizing carbon, and the solution allowed to stand for forty-eight hours. The crystals that have separated are filtered off, washed with ice water, and dried. Weight 220–230 g. The filtrate and washings are evaporated to 4.5 l. under reduced pressure in a 12-l. flask; 6.5 l. of methyl alcohol is added and the mixture allowed to stand in a cool place for twenty-four hours. The crystals that separate are filtered off, washed with cold water and dried, and an additional 150–160 g. is thus obtained. The total yield is 370–380 g. (76–78 per cent of the theoretical amount).

C. *Creatinine Picrate.* A mixture of 300 g. of commercial creatine hydrate with 190 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 50 cc. of water is warmed in a glass or porcelain dish on a steam bath for twenty-four hours. The resulting mass of creatinine hydrochloride crystals is dissolved in 1 l. of water, boiled with a little decolorizing carbon, and filtered. The solution is then diluted to 4 l. with distilled water, and heated to boiling in a 12-l. flask under a reflux condenser. To the hot solution is added, with good stirring, a solution of 500 g. of technical picric acid (containing 10 per cent of water) in 1250 cc. of warm methyl alcohol. Stirring is continued for one hour on the steam bath and the solution allowed to cool. The crystalline precipitate of creatinine picrate is filtered off, washed well with cold water, and dried. It forms long needles which melt at 220°; the melting point (Note 5) is unchanged on recrystallization from hot water. The yield is 620–630 g. (89–90 per cent of the theoretical amount).

## 2. Notes

1. As a rule, the commercial product, which contains one mol of water of crystallization, is entirely satisfactory; but if it is dark in color, it may be recrystallized from water with the use of decolorizing carbon.

2. Creatinine dissolves readily in pure water but is only slightly soluble in cold concentrated ammonia, while ammonium chloride is freely soluble.

3. The creatinine so prepared is practically 100 per cent pure; its recrystallization, while not recommended, may be carried out by dissolving, as rapidly as possible, 1 part by weight in 5 parts of water previously warmed to 65°, and then immediately adding to the warm solution double its volume of acetone, chilling in ice, and filtering after a few hours. The product is finally washed with acetone and dried. About one-third is lost in the filtrate.

4. The yield could be slightly increased by so modifying the conditions that the total volume of filtrate would be smaller, but this would involve an undue amount of trouble.

5. Special attention was given to the melting point determination, since two values, 205° and 212–213°, have been recorded in the literature.

### 3. Other Methods of Preparation

Creatinine has been prepared generally from urine [1] or muscle,[2] though its formation from creatine by the action of mineral acids has also been studied.[3] The conversion of creatine into creatinine has also been effected by heating in an autoclave [4] and by treatment with zinc chloride.[5] The above technique has been developed [6] since creatine has become available in relatively large quantities as a by-product.[7]

[1] Ann. **119**, 39 (1861); **159**, 279 (1871).
[2] Gazz. chim. ital. **17**, 382 (1887).
[3] Ann. **62**, 298 (1847); J. Am. Chem. Soc. **45**, 2242 (1923).
[4] J. Biol. Chem. **8**, 399 (1910).
[5] Jahresb. **1857**, 544; J. Biol. Chem. **18**, 183 (1914).
[6] J. Biol. Chem. **56**, 3, 881 (1923).
[7] J. Ind. Eng. Chem. **14**, 984 (1922).

# VIII

# CUPFERRON

$$C_6H_5NHOH + C_4H_9ONO + NH_3 \rightarrow C_6H_5N(NO)ONH_4 + C_4H_9OH$$

Prepared by C. S. MARVEL.
Checked by OLIVER KAMM.

## 1. Procedure

THE moist phenylhydroxylamine obtained from 1000 g. of nitrobenzene, by the method described on page 57, is weighed and dissolved in 4.5 l. of ordinary ether (Note 1). The ether-insoluble material (sodium chloride and water) is also weighed, the difference between the two weighings being a fairly accurate measure of the amount of phenylhydroxylamine in solution.

The ether solution is filtered through a dry filter paper into a 5-l. round-bottom flask which is fitted with an efficient mechanical stirrer and immersed in an ice-salt bath. When the temperature of the solution has fallen to 0° (Note 2), a rapid stream of dry ammonia gas, from a cylinder of compressed gas, is passed into the solution.

After about fifteen minutes, the theoretical amount of freshly distilled *n*-butyl nitrite (95 g. for every 100 g. of phenylhydroxylamine) is added slowly through a dropping funnel (Note 3). The addition of butyl nitrite usually requires about one hour (Note 4), during which time the stream of ammonia gas is continued in order that ammonia may always be in excess. If this precaution be not observed, a colored product will result. The temperature of the reaction mixture should be maintained below 10° and this may be done best by controlling the rate at which the butyl nitrite is added. An appreciable rise in tem-

perature will cause the volatilization of considerable quantities of ether and of ammonia (Note 5).

After the butyl nitrite has been added, the reaction mixture is stirred for about ten minutes longer in order to insure completion of the reaction, after which the cupferron is filtered off and washed several times with small portions of fresh ether. The product is spread on sheets of paper until all traces of ether have been lost, and is then stored in bottles where it is exposed to the vapors of ammonium carbonate. This may be done by protecting each cork with a double sheet of filter paper and placing a lump of ammonium carbonate between the cork and the filter paper.

The yield of cupferron from a given weight of phenylhydroxylamine averages 85–90 per cent of the theoretical amount.

## 2. Notes

1. The solvent ether may be replaced by benzene, but this modification offers no advantages for the preparation of cupferron on a laboratory scale.

2. The temperature must be kept low. If it is not, the material is generally colored brown and the reaction does not run smoothly. Probably the most important factor in securing successful results is always to have an excess of ammonia present.

3. The butyl nitrite is freshly distilled as a general precaution, because a product which has stood for some time is often partially decomposed.

4. In the preparation of cupferron, it has been recommended that the butyl nitrite be added all at one time. This procedure is satisfactory only when the amount of phenylhydroxylamine used is less than 200 g.; otherwise the reaction becomes extremely vigorous and an excessive proportion of ether is lost. The directions given above, on the other hand, are adaptable for the preparation of large quantities of cupferron. For the rapid preparation of small quantities of material, the butyl nitrite may be added all at one time, provided sufficient excess of ammonia is present.

5. It is found that 75 per cent of the ether and 95 per cent of the butyl alcohol used may be recovered, and that one man, working six to seven hours, is able to prepare 800 g. of cupferron. The recovered ether may be used over again, provided the following procedure is followed: The phenylhydroxylamine is dissolved in a little fresh ether, the solution cooled and treated with ammonia, then the recovered ether added. This precaution is necessary owing to the presence of some butyl nitrite in the recovered ether.

### 3. Other Methods of Preparation

Nitroso-β-phenylhydroxylamine, of which cupferron is the ammonium salt, has been made by the action of sodium nitrite and hydrochloric acid on β-phenylhydroxylamine,[1] of hydrogen peroxide on normal phenyldiazotates,[2] of sodium alcoholate and hydroxylamine on nitrobenzene,[3] of nitric oxide on phenyl magnesium bromide,[4] and by the action of permonosulfuric acid on aniline in the presence of amyl nitrite.[5]

Cupferron has usually been prepared from a mixture of alkyl nitrite and β-phenylhydroxylamine in the presence of ammonia in ether or benzene solution,[6] but it has also been made by the zinc dust reduction of nitrobenzene in the presence of amyl nitrite and ammonium hydroxide solution.[7]

[1] Ber. **27**, 1435, 1554 (1894); **52B**, 1839 (1919); J. Am. Chem. Soc. **41**, 280 (1919).

[2] Ber. **42**, 3575 (1909).

[3] Ber. **29**, 1885 (1896).

[4] Ann. **329**, 191 (1903).

[5] D. R. P. 227,659; Frdl. **10**, 126 (1910).

[6] Chem. Z. **35**, 913 (1911); J. Ind. Eng. Chem. **3**, 629 (1911); **12**, 799 (1920); J. Am. Chem. Soc. **41**, 280 (1919).

[7] D. R. P. 227,659; Frdl. **10**, 126 (1910).

# IX

## DI-*p*-TOLYLETHANE (*unsym.*)

$$2C_6H_5CH_3 + CH{\equiv}CH(HgSO_4) \rightarrow (CH_3C_6H_4)_2CHCH_3$$

Prepared by J. S. REICHERT and J. A. NIEUWLAND.
Checked by OLIVER KAMM.

### 1. Procedure

A 2-l. flask, containing 700 cc. of toluene, 70 cc. of concentrated sulfuric acid, and 7 g. of mercuric sulfate, is fitted with a stirrer, a thermometer reaching into the liquid, and an inlet tube connected with a gasometer containing acetylene, as shown in Fig. 1 (Note 1). The flask and its contents are tared and cooled to 10° before the absorption of acetylene is begun. The gas from the tank, *A*, is washed free from acetone by being passed first through water in the gasometer, *B*, and then through the concentrated sulfuric acid wash bottle, *C*.

The acetylene is absorbed rapidly, with the evolution of considerable heat. The temperature of the reaction mixture is maintained at 10–15° by immersing the flask in a freezing mixture. When at intervals the reaction slows down, it becomes necessary to sweep the system free from air which accumulates in the flask. The absorption is continued until about 60 g. of acetylene has been absorbed, which requires a period of about two hours (Note 2). During the absorption, the mixture turns first a reddish brown, then a dark brown, and finally almost black.

The reaction mixture is freed from the acid by washing once with pure water and then with sodium carbonate solution, to which some sodium chloride is added to aid the separation of

the hydrocarbon layer. If emulsification takes place, the addition of ether will remedy the difficulty.

The toluene layer is transferred to a 1-l. flask, without drying, and the unchanged toluene distilled off; the ditolylethane is then collected over a range of 295–310°. There is practically no intermediate fraction, but a tarry residue of about 75 g. remains in the flask. Upon redistillation, the ditolylethane is

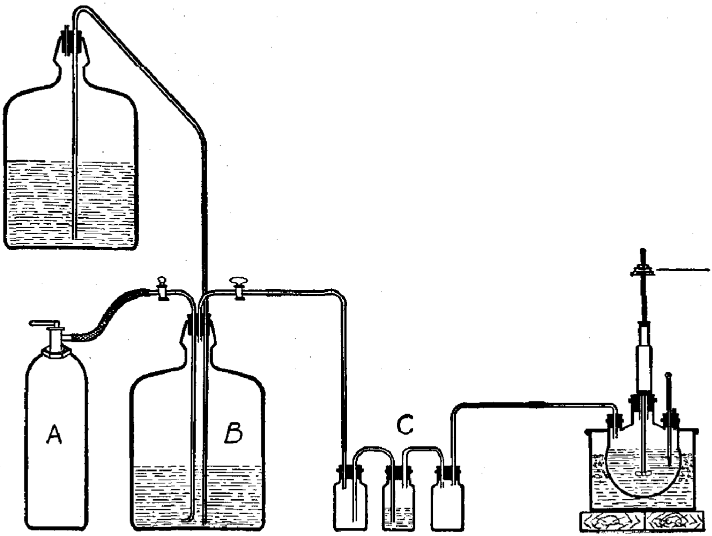



FIG. 1.

collected at 295–300°. The yield is 290–310 g. (60–64 per cent of the theoretical amount) (Note 3).

## 2. Notes

1. The acetylene is absorbed with unexpected rapidity so that it is unnecessary to deliver the gas beneath the surface of the liquid. In an ordinary reaction involving a gas it would be advisable to use a special stirrer of the type illustrated in Org. Syn. **3**, p. 29, and to deliver the gas beneath the distributing tube of the stirrer.

2. It is scarcely necessary to remove the flask for weighing until near the end of the experiment, since the volume of acetylene is known and practically complete absorption takes place. If a tank of compressed gas is not available, the acetylene may be prepared from calcium carbide by the usual laboratory methods.[1]

3. Subsequent redistillation yields a product boiling practically over a 2-degree range. The best product was obtained by a final fractionation under diminished pressure, when the boiling point was found to be 144–145°/8 mm.

4. Xylene, mesitylene, ethylbenzene, and benzene condense with acetylene in a manner similar to that described above for toluene, although the yields are usually lower.[2]

## 3. Other Methods of Preparation

Ditolylethane has been obtained also from the reaction between paraldehyde and toluene in the presence of sulfuric acid,[3] from the reaction between ethylidene chloride and toluene in the presence of aluminium chloride,[4] and by heating $\alpha$-ditolylpropionic acid in the presence of lime.[5]

[1] Cf. C. A. **3**, 2887 (1909).
[2] J. Am. Chem. Soc. **45**, 3090 (1923)
[3] Ber. **7**, 1193 (1874).
[4] Ann. **235**, 313 (1886).
[5] Ber. **15**, 1476 (1882).

# ETHYL OXOMALONATE

$$CH_2(CO_2C_2H_5)_2 + 2N_2O_3 \rightarrow CO(CO_2C_2H_5)_2 + H_2O + 4NO$$

Prepared by A. W. Dox.
Checked by C. S. Marvel and R. L. Shriner.

## 1. Procedure

Into a 500-cc. Erlenmeyer flask containing 200 g. of ethyl malonate, and cooled to 0° by surrounding with cracked ice and salt, a rapid current of nitrous anhydride is passed. The gas is generated by dropping concentrated nitric acid through a separatory funnel upon dry arsenious oxide contained in a 500-cc. Florence flask placed upon a tripod and wire gauze. The arsenious oxide should be in lumps about the size of a pea. An empty flask is inserted between the generator and the absorption flask and the gas dried by passage through a calcium chloride tube (Note 1). As the evolution of gas slows down, gentle heat may be applied with a burner. The ethyl malonate becomes dark green in color. There should be an increase in weight of about 200 g. in two to three hours.

The liquid is left in the freezing mixture for several hours, then gradually allowed to come to room temperature (Note 2). Red gases are slowly evolved. After standing for two days or more at room temperature, the liquid is transferred to a distilling flask provided with a capillary air intake, and the delivery tube connected with a water-cooled condenser and receiver. The distillation is performed under diminished pressure, by the use of a water pump. Considerable nitric oxide is evolved before the pressure drops to about 70 mm. (Note 3).

The first fraction consists mainly of water, a little ethyl acetate, and some ethyl oxomalonate which recombines with the water to form ethyl mesoxalate. When the pressure has dropped to 45 mm. and the temperature has risen to 110°, the receiver is

changed (Note 4). The main product, ethyl oxomalonate, now distils at 110–135°/45–50 mm. If the oxidation has been complete, very little residue is left (Note 5). Redistillation gives a golden-yellow liquid boiling between 103–108°/15 mm. The yield is 160–165 g. (74–76 per cent of the theoretical amount).

## 2. Notes

1. The yield of ethyl oxomalonate is decreased if the nitrous anhydride is not dried.

2. If the temperature is raised too rapidly, the liberation of gases causes the mixture to boil too vigorously.

3. A motor pump is not recommended because the nitric oxide is apt to cause corrosion. If too high a vacuum is used at first, a residue of ethyl iso-nitrosomalonate may remain.

4. The remainder of the distillation must be conducted with extreme care. As soon as the ethyl oxomalonate has partly distilled over and the temperature has risen somewhat, the remaining iso-nitroso compound begins to decompose and sometimes liberates gases so rapidly that the thermometer and capillary tube may be blown out of the flask. If the manometer is watched closely, and at the first sign of liberation of gas, as evinced by a sudden increase in pressure, a wet towel is placed around the flask, the reaction can be slowed down.

5. In case any considerable amount of residue remains above 135° at 45 mm., it is heated at ordinary pressure to a higher temperature until no more nitric oxide is given off, then distilled as before.

## 3. Other Methods of Preparation

Ethyl oxomalonate is obtained from a variety of intermediates[1] but the only method which appears of practical value consists in the oxidation of ethyl malonate by means of oxides of nitrogen. This reaction, carried out in two steps by Bouveault and Wahl,[2] was studied by Schmidt[3] and subsequently considerably improved by Curtiss[4] and also by Meyer.[5]

[1] Beilstein, **3**, 769–770 (Fourth Edition). [2] Compt. rend. **137**, 196 (1903).
[3] Compt. rend. **140**, 1400 (1905). [4] Am. Chem. J. **33**, 603 (1905); **35**, 477 (1906).
[5] Bull. soc. chim. (4) **9**. 423 (1911); C. A. **5**. 3220 (1911).

# ETHYL PROPANE-1,1,2,3-TETRACARBOXYLATE

$$CH_2(CO_2C_2H_5)_2 + CH(CO_2C_2H_5){-}CHCO_2C_2H_5 + (C_2H_5ONa) \rightarrow CH(CO_2C_2H_5)_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5$$

Prepared by H. T. Clarke and T. F. Murray.
Checked by C. S. Marvel and M. M. Brubaker.

## 1. Procedure

In a 5-l. flask, fitted with a stirrer, reflux condenser, and dropping funnel, is placed 1000 g. of absolute ethyl alcohol; 92 g. of sodium, cut into strips, is then added through the condenser at such a rate that the alcohol does not boil too vigorously. When all the sodium is in solution, the flask is cooled and 800 g. of ethyl malonate added through the condenser, with stirring. The mixture is warmed gently on the steam bath and 700 g. of ethyl fumarate (Note 1) added from the dropping funnel. During this addition the solution is kept boiling gently, heat being applied if necessary (Note 2). The mixture is boiled for one hour after the ethyl fumarate has been added. It is then cooled and 250 g. of glacial acetic acid is added.

Most of the alcohol is distilled off under slightly reduced pressure on the steam bath and the residue is poured into sufficient distilled water to dissolve all the solid. The water layer is separated and extracted four times with carbon tetrachloride, which is added to the ester layer. The ester-carbon tetrachloride mixture is washed twice with water and the water washings extracted once with carbon tetrachloride. The carbon tetrachloride is distilled off under atmospheric pressure through a column, the moisture being carried over simultaneously.

The residue is then distilled under reduced pressure, when the ethyl propane-1,1,2,3-tetracarboxylate comes over at 182–184°/8 mm. The yield is 1261–1273 g. (95–96 per cent of the theoretical amount).

## 2. Notes

1. The ethyl malonate and ethyl fumarate should be redistilled under reduced pressure, and the material boiling over a 2-degree range should be collected.

2. Heat is developed during the reaction, and the mixture may be kept boiling by adding the ethyl fumarate at a suitable rate.

## 3. Other Methods of Preparation

Now that fumaric and maleic acid are available commercially, the most convenient method of preparing the above ester consists in condensing ethyl malonate with ethyl fumarate[1] or ethyl maleate.[2] It has also been prepared by condensing malonic ester with ethyl chlorosuccinate[3] and with ethyl ethoxysuccinate.[4]

[1] Ber. **24**, 2889 (1891); J. prakt. Chem. (2) **45**, 56 (1892); J. Chem. Soc. **73**, 1007 (1898); Ann. **341**, 102 (1905).

[2] J. prakt. Chem. (2) **45**, 56 (1892).

[3] Ber. **23**, 3759 (1890).

[4] Chem. Zentr. **1903** (II), 943; Ann. **341**, 104 (1905).

XII

# GLYCINE

$$CH_2{=}NCH_2CN + 3H_2O + 2HBr \rightarrow CH_2O + HBr \cdot NH_2CH_2CO_2H + NH_4Br$$

$$HBr \cdot NH_2CH_2CO_2H + C_5H_5N \rightarrow NH_2CH_2CO_2H + C_5H_5N \cdot HBr$$

Prepared by H. T. Clarke and E. R. Taylor.
Checked by Roger Adams and W. F. Tuley.

## 1. Procedure

In a 5-l. flask fitted with a downward condenser, are placed 340 g. of methylene aminoacetonitrile (p. 47) and 2500 g. of 48 per cent hydrobromic acid (Note 1). The mixture is heated on the steam bath for three hours (Note 2). The pressure in the apparatus is then reduced and dilute acid and formaldehyde are distilled into a water-cooled receiver until the separation of ammonium bromide from the reaction mixture causes bumping. This occurs when approximately half of the liquid has been distilled over. The ammonium bromide is filtered from the hot liquid and washed with a small amount of cold water; the filtrates are returned to the flask and distillation continued as nearly as possible to dryness (Note 3). The residue is dissolved in 2 l. of cold methyl alcohol and filtered; to the filtrate is added 350 cc. of pyridine, with vigorous shaking (Note 4).

The mixture is allowed to stand over night and the precipitated glycine filtered off and washed with methyl alcohol (Note 5) until the washings are free from bromides. The product is dissolved in 300 cc. of boiling distilled water and the solution filtered with the use of a little decolorizing carbon; the filtrate is allowed to cool to 40–50°, when 1500 cc. of methyl alcohol is added with hand stirring. If the product is colored, the procedure, just described, of dissolving in water and reprecipitating with methyl alcohol is repeated. The glycine that

separates is filtered off when the mixture is cold and washed with methyl alcohol until a sample (Note 6) is found to be free from ammonia on testing with Nessler solution (Note 7). If a second precipitation is made, the glycine is practically free from ammonium salts and washing with methyl alcohol is unnecessary. Not more than 1 l. of methyl alcohol should be necessary for this purpose; if positive tests continue to be obtained, an ammonia-free product may be secured by treating the aqueous solution for a short time with a water-softening zeolite, filtering and crystallizing or precipitating with alcohol.

The yield is 115–140 g. (31–37 per cent of the theoretical amount) of a colorless product which melts with decomposition at 225–230° (Note 8).

The distillate from the reaction mixture may be redistilled under atmospheric pressure with the use of a column; the fraction boiling at 125–126° may be collected, when one-third to one-half the amount of hydrobromic acid originally taken can be recovered. The foreruns contain formaldehyde.

## 2. Notes

1. If preferred, 3000 g. of 40 per cent acid may be taken. Hydrobromic acid is employed in preference to other mineral acids on account of the high solubility of ammonium bromide in methyl alcohol.

2. Hydrolysis takes place readily, with a slight evolution of heat, so that actual boiling over a free flame is unnecessary.

3. The residue consists of a syrup (largely glycine hydrobromide) mixed with crystals of ammonium bromide. It has a strong odor of formaldehyde.

4. A technical grade of pyridine may be employed if this is colorless and distils not lower than 100° nor higher than 140°.

5. Ammonium bromide dissolves in about eight times its weight of methyl alcohol. It is much less soluble in absolute ethyl alcohol, requiring about 30 parts of that solvent.

6. The sample should be taken from the lower part of the cake on the funnel by means of a glass tube, since the upper layers become free of impurities first.

7. The sample of glycine must be dry before testing, as traces of impurities generally present in the methyl alcohol give a precipitate with Nessler solution. To carry out the test, 0.1–0.2 g. of dry product is dissolved in 3 to 5 cc. of distilled water containing a few drops of sodium hydroxide solution, and 1 cc. of Nessler solution is added.

8. A further small quantity of impure glycine can be isolated by concentrating the filtrates obtained on recrystallization. The liquors from the first precipitation, containing ammonium bromide, pyridine hydrobromide, excess pyridine, and alcohol-soluble by-products, may be treated as follows: The mixture is first acidified with mineral acid and the methyl alcohol recovered by distillation with a column. The residue is rendered strongly alkaline and the bulk of the ammonia removed by boiling under a reflux condenser; wet pyridine can be recovered by downward distillation and treatment of the distillate with solid sodium hydroxide.

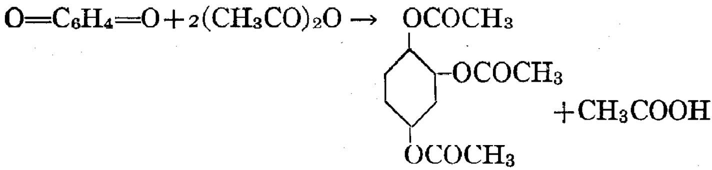
### 3. Other Methods of Preparation

Glycine hydrochloride has been prepared by the action of hydrochloric acid upon hippuric acid,[1] upon aminoacetonitrile,[2] upon methylene aminoacetonitrile,[3] and upon ethyl phthaliminoacetate;[4] its conversion into free glycine by methods involving silver or lead oxides is apt to be troublesome. The classical method of preparing glycine by the interaction of chloroacetic acid and ammonia[5] is unsatisfactory, owing to the laborious process of isolation through the copper salt, which, moreover, rarely gives a product entirely free of ammonia. The hydrolysis of methylene aminoacetonitrile by successive treatments with barium hydroxide and sulfuric acid[6] furnishes a more satisfactory method, but the final product is seldom entirely pure, partly owing to the difficulty in obtaining pure barium hydroxide. The same objection applies to the hydrolysis of aminoacetonitrile by means of barium hydroxide.[7]

1 J. prakt. Chem. (2) **37**, 157 (1888).
2 Ann. **278**, 236 (1894).
3 Ber. **27**, 60 (1894).
4 Ber. **22**, 428 (1889).
5 Ann. **266**, 295 (1891).
6 Biochem. J. **16**, 702 (1922).
7 Ann. **278**, 237 (1894).

# XIII

## HYDROXYHYDROQUINONE TRIACETATE




Prepared by E. B. Vliet.
Checked by Roger Adams and H. O. Calvery.

### 1. Procedure

Twelve grams of concentrated sulfuric acid is added to 180 g. of acetic anhydride in a 600-cc. beaker, after which 60 g. of benzoquinone (Note 1) is added gradually in small portions with constant mechanical stirring. The temperature rises and should be held at 40–50° during the addition of the quinone. A temperature higher than 50° leads to decomposition of the product while a temperature lower than 40° causes a much slower reaction. Good temperature control can be obtained by using care in adding the quinone and by the use of a cooling bath and efficient stirring. The reaction goes smoothly and does not evolve an excessive amount of heat.

After all the quinone has been added, the solution is allowed to stand. It should be watched closely at first to see that the temperature does not rise above 50°, but at the same time it is well not to cool it below 40°. When the mixture starts to cool of its own accord, a precipitate begins to form. As soon as the mixture has cooled to about 25° (Note 2), it is poured into 750 cc. of cold water, whereupon a white precipitate separates. This is cooled to about 10° and filtered off with suction. The

product is recrystallized from 250 cc. of 95 per cent ethyl aclohol and dried. The drying is best done in a vacuum desiccator, through which a very small stream of air is allowed to sweep. Calcium chloride is the best drying agent.

The product is practically white and rather granular; it melts at 96–97°. The yield is 120–123 g. (85–87 per cent of the theoretical amount). The product is fairly reactive and tends to decompose upon standing (Note 3), especially if care be not used in drying and handling. If it is to be used as a starting material for other syntheses, it is advisable to use it as soon as possible.

## 2. Notes

1. The quality of the product depends to a large extent upon the purity of the benzoquinone; if the latter is dark, it is advisable to crystallize it from benzene before using it. (See Org. Syn. **2**, 86.)

2. It is quite desirable to have the reaction mixture cooled to about 25° before it is added to the water. If it is warm when added to the water, an oil will separate which solidifies slowly in the form of lumps.

3. The hydroxyhydroquinone triacetate keeps quite satisfactorily in an atmosphere of carbon dioxide.

## 3. Other Methods of Preparation

The method described above is essentially the same as that of Thiele,[1] which has been patented by F. Bayer and Company.[2] Hydroxyhydroquinone triacetate has also been obtained by acetylating hydroxyhydroquinone formed by the alkali fusion of hydroquinone.[3]

[1] Ber. **31**, 1247 (1898); Gazz. chim. ital. **40** (2) 349 (1910).
[2] D. R. P. 101,607 and 107,508; Frdl. **5**, 155–6 (1898).
[3] Monatsh. **5**, 590 (1884).

XIV

## o-IODOPHENOL

$$2HOC_6H_4HgCl + 2I_2 \rightarrow HgI_2 + HgCl_2 + 2IC_6H_4OH$$

Prepared by F. C. WHITMORE and E. R. HANSON.
Checked by J. B. CONANT and R. M. GRANARA.

### 1. Procedure

A 2-l. round-bottom short-neck flask is equipped with a glass mechanical stirrer. A suspension of 165 g. of *o*-chloromercuriphenol (p. 13) (m.p. 147° or higher) in 500 cc. of chloroform is placed in the flask and treated with 127 g. of iodine, the stirring being continued until a small sample on filtration shows no unreacted iodine. This requires from one to two hours. The solid inorganic mercury compounds are removed by suction filtration. The filtrate is distilled from a 1-l. distilling flask on the water bath to remove most of the chloroform, which is saved for later runs (Note 1). The residual liquid is shaken vigorously with a solution of 5 g. of potassium iodide in 10 cc. of water, to remove dissolved mercuric iodide. The heavier layer, which still possesses a reddish color, is transferred without drying to a 200-cc. Claisen flask and distilled under diminished pressure. At first a small amount of chloroform and water distils over, after which the higher-boiling material is collected in a separate receiver. Small amounts of inorganic mercury compounds remain in the flask (Note 2).

The *o*-iodophenol solidifies upon cooling. The yield of material melting at 32–34° is 70 g. (63 per cent of the theoretical amount). The product obtained in this way is slightly yellow. If a purer product is desired, it may be redistilled *in vacuo.*

Most of the crude material will distil over a 5-degree range (b.p. 130°/18 mm. and 186°/160 mm., m.p. 43°).

## 2. Notes

1. About 460 cc. of chloroform can be recovered, the time required being one hour.

2. The first distillation of the iodophenol should be carried out under a good vacuum, 40 mm. or lower. The redistillation may be conducted at a higher pressure if desired.

3. Since the iodophenol has a most persistent odor, care should be exercised in working with it. A solution of bromine in glycerol may be used as an antidote for burns from the iodophenol (p. 14).

## 3. Other Methods of Preparation

*o*-Iodophenol has been made by diazotization from *o*-aminophenol [1] and from *o*-iodoaniline.[2] It has been obtained by heating *o*-iodosalicylic acid.[3] Mixed with its para isomer and diiodophenol, it has been made by treating a dilute phenol solution with iodine and iodic acid,[4] and it has also been obtained from an alkaline solution of phenol and iodine in the presence of mercuric oxide,[5] and from dry sodium phenolate and iodine in carbon disulfide.[6]

[1] Ber. **8**, 820 (1875); Ann. **241**, 68 (1887).
[2] Chem. Zentr. **1910** (II), 304.
[3] Ann. **120**, 315 (1861).
[4] Z. Chem. **1866**, 662; **1868**, 322.
[5] Ber. **2**, 523 (1869); **6**, 1251 (1873).
[6] Ber. **16**, 1897 (1883); **20**, 3363 (1887).

# XV

## KETENE

$$CH_3COCH_3 \rightarrow CH_2{=}CO + CH_4$$

Prepared by C. D. Hurd.
Checked by Oliver Kamm.

### 1. Procedure

A. *Preparation of ketene.* The arrangement of the apparatus is shown in Fig. 2 (Note 1). The graduated separatory funnel, shown in the diagram, filled with 125 cc. of commercial acetone, leads into a 500-cc. round-bottom flask which, in turn, is connected by gas-tight joints (Note 2) to a glass combustion tube filled with broken porcelain, a spiral or bulb condenser, a two-way stopcock, and a reaction flask. In the reaction flask is placed the material with which the ketene is to react (Note 3). A second reaction flask may be placed in series, if desired, to ascertain if any ketene escaped reaction in the first flask.

Prior to either of these steps, fourteen of the twenty burners of the combustion furnace are lighted (Note 4) and tiles are placed over the lighted burners, which finally must be adjusted to yield a maximum temperature. The first two and last four burners are unused.

When the furnace is fully heated, boiling water is placed beneath the round-bottom flask and cold water passed through the condenser. Acetone is now dropped in at the rate of 3–4 cc. per minute. About half the acetone should be recovered as distillate in cylinder *B* (Note 5). Ketene, admixed with methane, carbon monoxide, and ethylene, passes into the reaction flasks (Note 6) in 25–29 per cent yields. The flow may be interrupted at will by checking the acetone flow.

B. *Preparation of acetanilide.* Since ketene is a highly reactive gas, it is usually prepared for immediate consumption instead of being isolated as such. It reacts with various groups which contain hydrogen, such as hydroxyl, amino, mercaptan, hydroxylamino, etc., forming acetyl derivatives.

Twenty-five grams of aniline is placed in the reaction flask, *D*, and 50 cc. of dry ether added as solvent (Note 7). A second reaction flask is connected at *C*, in which is placed 5 g. of aniline,

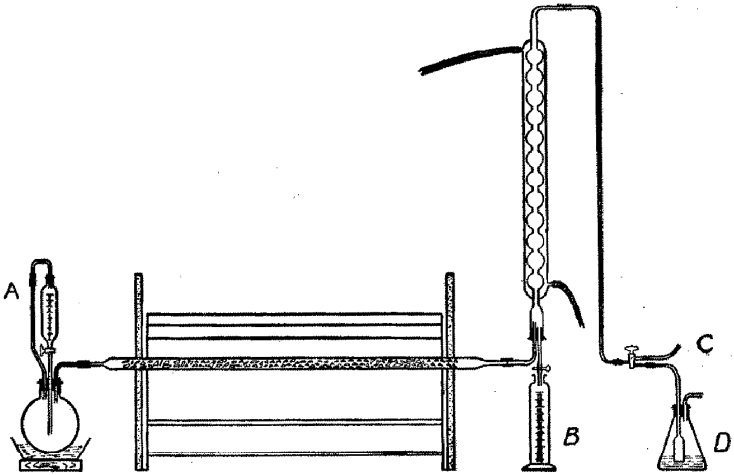



FIG. 2.

dissolved in 20 cc. of ether. This prevents the escape of ketene vapor at the beginning and at the close of the operation (Note 5). In all, 85 cc. of acetone is passed through the apparatus, 39 cc. of which is recovered as distillate. Therefore, 44 cc. (or 35 g.) of acetone is decomposed. The duration of the run is about thirty minutes. Twenty-one grams of acetanilide, which corresponds to a yield of 25.8 per cent, based upon the amount of acetone decomposed, is isolated from the reaction mixture.

## 2. Notes

1. *The apparatus.* A graduated dropping funnel and a graduated cylinder for the distillate are chosen because of convenience in determining the volume of decomposed acetone.

The bulb (or spiral) condenser is chosen because of its efficiency. With an ordinary condenser, it is necessary to insert two U-tubes, cooled by ice, between the condenser and the reaction flask, to remove all the acetone from the ketene. In many reactions, however, this admixed acetone will do no harm. This part of the apparatus is designed to eliminate the loss of ketene by solvent action, prior to its entry into the reaction flask.

A wide-mouth delivery tube in the reaction flask is essential to prevent clogging, when a solid product is formed. Automatic stirring in the reaction flask may be used to advantage in certain instances. There is constant agitation, of course, as the gaseous decomposition products bubble through.

Either Scotland glass or Pyrex is satisfactory for the combustion tube. An estimate of the temperature is 650° (Note 4). The life of the tube is lengthened if it rests upon a layer of thin asbestos paper. The tube is filled with pieces of broken porcelain, to serve as a " heat reservoir "; there is no catalytic effect. The porcelain blackens during the reaction.

2. *Care in assembly.* Since this is a gaseous reaction, it is essential that the apparatus be free from leaks; thus, corks are eliminated wherever possible. The ends of the combustion tube and the top of the condenser are drawn to the diameter of the connecting tubes and joined by a piece of thick-walled rubber tubing. Care should be taken to have the ends of the glass tubes come into contact. The rubber tube situated between the furnace and condenser is protected by the asbestos screen, but a further essential precaution is taken, namely, that this end of the combustion tube extend a considerable distance from the furnace.

The stoppers in the reaction flask and at the top of the dropping funnel are of rubber; the other two are well-selected corks, bored perfectly and painted both inside and out with waterglass, one day previous to being used.

3. The apparatus may be calibrated by allowing the ketene to react with 5N alkali and titrating the excess alkali with acid.

4. With an electric combustion furnace, wherein a tempera-

ture of 695–705° is maintained, consistent yields of 35–40 per cent ketene are produced. The best rate of flow in such a case is 4–6 cc. per minute, with recovery of 60–80 per cent of the original acetone as distillate. Although yields of ketene ranging above 45 per cent have been obtained frequently with this apparatus, they could not be duplicated consistently.

5. The thermal decomposition of ketene into carbon monoxide and ethylene is prevented, as far as possible, by the rapid removal of ketene from the hot tube, which is accomplished by the undecomposed acetone vapor. About half the acetone originally used should be collected unchanged as distillate by the vertical condenser. The yield of ketene will fall considerably if less distillate is formed.

6. Ketene gas is very irritant when breathed, and hence proper cautions should be taken to avoid inhalation.

7. An ice bath surrounding the reaction flask is usually employed, not only to prevent the vaporization of the solvent, but also to promote a greater solubility of ketene.

### 3. Other Methods of Preparation

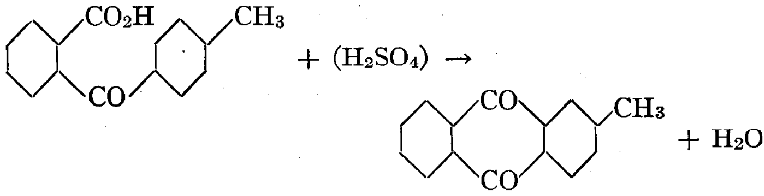
In addition to the above method, based upon the work of Schmidlin and Bergman [1] as modified by Hurd and Cochran,[2] ketene has been prepared by the pyrogenic decomposition of acetic anhydride,[3] of ethyl acetate, and of triacetin.[4] In the last instance, acrolein and acetic acid are formed simultaneously.

Ketene has also been formed by the action of zinc upon an ethereal solution of bromoacetyl bromide.[5] Carbon monoxide and diazomethane, diluted with ether, when passed through a quartz tube at 400–500°, yield ketene and nitrogen.[6]

[1] Ber. **43**, 2821 (1910).
[2] J. Am. Chem. Soc. **45**, 515 (1923).
[3] J. Chem. Soc. **91**, 1938 (1907); **97**, 1968 (1910).
[4] Ber. **47**, 2393 (1914).
[5] Ber. **41**, 594 (1908).
[6] Ber. **45**, 508 (1912).

XVI

## β-METHYL ANTHRAQUINONE



Prepared by L. F. Fieser.
Checked by ROGER ADAMS and R. L. SHRINER.

### 1. Procedure

THE *p*-toluyl-*o*-benzoic acid which is obtained from 100 g. of phthalic anhydride (p. 73), and which should weigh 157 g., is mixed with 1400 g. of fuming sulfuric acid (20 per cent anhydride) (Note 1) in a 2-l. flask protected by a calcium chloride tube; and the mixture is heated on the steam bath for two hours with occasional shaking (Note 2). The clear, deep red solution is poured when cold upon cracked ice in a 4-l. beaker. The methyl anthraquinone separates and is digested for twenty minutes by passing in steam, after which it is filtered by suction. A flannel cloth is used in the filter, or a filtros plate may be cemented into a Büchner funnel with water-glass. The precipitate is washed well with hot water, after which it is returned to the beaker and digested as before with hot water to which is added a slight excess of ammonia, beyond that required to neutralize any acid present.

The product is filtered and dried to constant weight. The filtrate will be clear and will give no precipitate with hydrochloric acid if the conditions of condensation have been correct.

The β-methyl anthraquinone is pale tan in color and weighs from 118 to 130 g. (86–95 per cent of the theoretical amount, based upon the weight of acid taken). It is practically pure, melting at 173°. Upon crystallization from alcohol in the presence of bone-black, it forms long, silken, almost colorless needles, melting constantly at 173.5° (176° cor.).

## 2. Notes

1. Some investigators have used concentrated instead of fuming sulfuric acid for the condensation, but the yield is usually low and the product is always colored bright yellow by some impurity which cannot be removed by crystallization.

2. The time allowed for condensation may be shortened to one-half, without affecting the yield, by maintaining the temperature at 125–130° for this length of time.

## 3. Other Methods of Preparation

β-Methyl anthraquinone has been obtained by the oxidation of β-methyl anthracene by several investigators;[1] and material of the same origin, obtained by the benzene-extraction of crude commercial anthraquinone,[2] has been fully described. As regards the synthesis from phthalic anhydride and toluene, both the preparation and properties of *p*-toluyl-*o*-benzoic acid[3] and the complete synthesis[4] have been the subject of several papers. This acid has also been prepared from *o*-carbomethoxy benzoyl chloride and toluene.[5] The phthalic anhydride synthesis of anthraquinone derivatives in general has received considerable attention. An account of this work, together with extensive references, is given by Barnett.[6]

The following unimportant preparative methods may be mentioned: the production of β-methyl anthraquinone by the reduction of 2-bromo-3-methyl anthraquinone;[7] the oxidation of β-methyl anthracene-γ-carboxylic acid;[8] and the reduction of 2-methyl anthraquinonyl-1-diazonium sulfate.[9]

[1] Ber. **8**, 675 (1875); J. prakt. Chem. [2] **79**, 560 (1909); [2] **82**, 232 (1910); [2] **83**, 210 (1911); Ann. chim. phys. [8] **20**, 445 (1910).

[2] J. Chem. Soc. **65**, 843 (1894); Ber. **10**, 1485 (1877); **15**, 1820 (1882); **16**, 696, 1632 (1883).

[3] Bull. soc. chim. [2] **35**, 505 (1881); [3] **17**, 969 (1897); Ann. chim. phys. [6] **14**, 447 (1888); Monatsh. **32**, 639 (1911); J. Am. Chem. Soc. **43**, 1965 (1921).

[4] J. prakt. Chem. [2] **33**, 319 (1886); [2] **41**, 4 (1890); Ann. **234**, 239 (1886); **299**, 300 (1898); **311**, 180 (1900); Ber. **28**, 1134 (1895); **41**, 3632 (1908); J. Russ. Phys. Chem. Soc. **46**, 1067 (1914).

[5] J. Am. Chem. Soc. **43**, 1922 (1921).

[6] Anthracene and Anthraquinone, pp. 130–141, Van Nostrand (1921).

[7] Ber. **45**, 796 (1912).

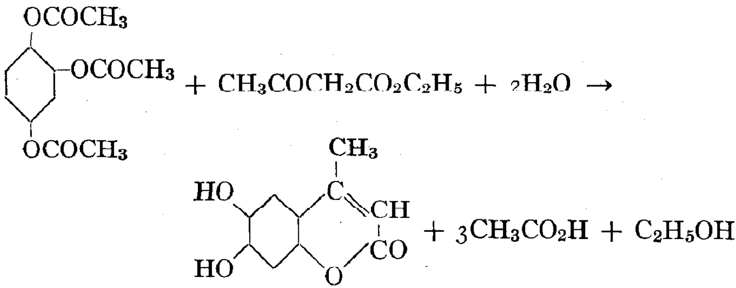
[8] Ber. **45**, 1214 (1912).

[9] Ber. **46**, 1646 (1913).

## XVII

# β-METHYL ESCULETIN

## (6, 7-Dihydroxy-4-methyl-1, 2-benzopyrone)



Prepared by E. B. Vliet.
Checked by Roger Adams and E. E. Dreger.

### 1. Procedure

A smooth, uniform paste is made by thoroughly mixing 60 g. of ethyl acetoacetate (Note 1) and 114 g. of hydroxyhydroquinone triacetate (p. 35). *This requires several minutes of* stirring. To this mixture is added 450 cc. of 75 per cent sulfuric acid (Note 2). The paste slowly dissolves with the evolution of heat, giving a deep red solution; the latter is heated on a warm bath with occasional stirring until it reaches 80°, at which temperature it is maintained for one-half hour. It is then allowed to cool to room temperature and poured into 1850 cc. of cold water. The resulting mixture is cooled to room temperature, filtered with suction, and the precipitate washed with cold water to free it from excess acid. The β-methyl esculetin thus obtained is dried at 100° and is generally gray in color. The yield is about 80 g. (92 per cent of the theoretical amount).

A pure product may be obtained by dissolving with the aid of heat and stirring 100 g. of β-methyl esculetin in a solution of 200 g. of borax in 700 cc. of water. The solution obtained is filtered while hot and then cooled, whereupon the esculetin borate separates (Note 3). This is filtered off and dissolved in 1800 cc. of water, and the solution thus obtained added to 50 g. of concentrated sulfuric acid in 500 cc. of water. β-Methyl esculetin separates and, after the mixture has been cooled, is filtered, washed, and dried. From 100 g. of the crude material, 85 g. of pure product melting at 272–274° (uncor.) is obtained. This is generally nearly colorless but occasionally possesses a slight grayish tinge.

## 2. Notes

1. In order to obtain a fairly pure product without recrystallization, the intermediate ethyl acetoacetate and hydroxyhydroquinone triacetate must be pure.

2. It is important to use 75 per cent sulfuric acid in this reaction, because more concentrated acid gives a very dark product and a lower yield, while more dilute acid will not induce the reaction.

3. The exact nature of the precipitate has not been determined.

## 3. Other Methods of Preparation

β-Methyl esculetin was first prepared by Pechman,[1] by condensing hydroxyhydroquinone triacetate and ethyl acetoacetate by allowing them to stand for twenty-four hours with cold concentrated sulfuric acid. This method gave a dark product, difficult to purify, and a yield of 60–65 per cent. Pechman also used boiling alcoholic zinc chloride as the condensing agent in place of sulfuric acid but does not state the yield thus obtained.

Bargellini and Martegiani[2] used 73 per cent sulfuric acid and heated on the water bath. They obtained an improved yield of a product of better quality. Zinc chloride in acetic acid proved to be unsatisfactory.

[1] Ber. **34**, 423 (1901).

[2] Gazz. chim. ital. **41** (2), 613 (1911).

XVIII

## METHYLENE AMINOACETONITRILE

### ($\alpha$-Hydroformamine Cyanide *)

$$NaCN + NH_4Cl + 2HCHO \rightarrow CH_2{=}NCH_2CN + NaCl + 2H_2O$$

Prepared by ROGER ADAMS and W. D. LANGLEY.
Checked by H. T. CLARKE and E. R. TAYLOR.

### 1. Procedure

IN a 5-l. round-bottom flask, fitted with a mechanical stirrer and surrounded by an ice-salt bath, are placed 1500 cc. of technical formaldehyde (sp. gr. 1.078/20°) (Note 1) and 540 g. of ammonium chloride. A thermometer is placed in the liquid, which is cooled to 0°. This temperature is maintained throughout the entire reaction (Note 2). Stirring is commenced (Note 3) and a solution of 490 g. of 98 per cent sodium cyanide in 850 cc. of water is dropped into the mixture of ammonium chloride and formaldehyde at such a rate (about 90 drops per minute) that at least six hours will be required for this addition.

When one-half the sodium cyanide solution has been added, all of the ammonium chloride will be in solution. At this point, the addition of 380 cc. of glacial acetic acid is started at such a rate (2 to 2.5 cc. per minute) that the addition of both the acid and the remainder of the sodium cyanide solution will be completed at the same time. The methylene aminoacetonitrile begins to separate in white crystals shortly after the addition of the glacial acetic acid has commenced. After all the sodium cyanide solution and acetic acid have been added, the mixture is stirred for an hour and a half longer; then the precipitate

* The actual molecular formula is $C_9H_{12}N_6$. Johnson and Rinehart, J. Am. Chem. Soc. 46, 768, 1653 (1924).

is filtered off, transferred to a beaker, and stirred with 1.5 l. of water. The product is filtered with suction, washed with 500 cc. of water (Note 4), and dried on filter paper. The yield is 410 to 475 g. (64–74 per cent of the theoretical amount) of a product of which the melting point is 129° (Note 5).

## 2. Notes

1. The formalin contains 35 per cent formaldehyde by weight, as determined by specific gravity. It should contain no suspended paraformaldehyde.

2. During the reaction, the temperature should be kept as near 0° as possible and should never rise above 5°. If the temperature goes higher, a heavy oil is sometimes obtained instead of the crystalline product. It is not difficult to maintain the low temperature when the formaldehyde and ammonium chloride are cooled to 0° before any of the sodium cyanide is added.

3. In order to obtain good yields, the stirring must be vigorous throughout the entire reaction.

4. With careful washing, 500 cc. of cold water should be sufficient to remove all chlorides.

5. For most purposes, the product is pure enough as it is obtained from the reaction mixture, but it may be crystallized from water. This recrystallization is, however, attended with considerable loss.

## 3. Other Methods of Preparation

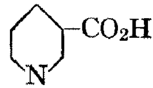
Methylene aminoacetonitrile has been prepared by the action of formaldehyde on aminoacetonitrile,[1] and by the action of formaldehyde on a mixture of ammonium chloride, potassium cyanide, and acetic acid.[2]

[1] J. prakt. Chem. (2) **65**, 192 (1902).

[2] Ber. **27**, 59 (1894); **36**, 1507 (1903); **43**, 868 (1910); J. Am. Chem. Soc. 768, 1653 (1924).

# XIX

## NICOTINIC ACID

$C_{10}H_{14}N_2 + (HNO_3) \rightarrow$ 

Prepared by S. M. McElvain.
Checked by J. B. Conant and B. B. Corson.

### 1. Procedure

In a 5-l. round-bottom flask is placed 4 kg. of c.p. concentrated nitric acid (sp. gr. 1.42) (Note 1). To this is added, in 25-cc. portions, 210 g. of nicotine (Note 2). The addition should be made carefully in order that local heating may not occur and material be lost. After each addition of nicotine, the flask should be shaken in order to insure a homogeneous solution. The addition of the nicotine causes the temperature of the liquid to rise somewhat but not sufficiently to cause evolution of nitrogen dioxide. The flask is placed on a steam bath under a hood and heated until the liquid reaches a temperature of 70°. It is then removed and the reaction allowed to continue spontaneously (Note 3), heat enough being evolved to cause the liquid to boil. The boiling ceases after one hour but the flask is replaced upon the steam bath for ten to twelve hours, during which time there is a more or less continuous evolution of oxides of nitrogen.

The contents of the flask are then poured into an evaporating dish and evaporated almost to dryness on the steam bath (about ten hours). The purification which follows is best carried out with the product of two runs such as have been described above.

After the evaporation of most of the liquid, the nicotinic acid nitrate from two runs is transferred to a 1.5-l. beaker, 400 cc. of distilled water is added (Note 4) and the mixture is heated until complete solution results. On cooling, the nicotinic acid nitrate separates as yellow granular crystals and is

filtered off. To obtain it absolutely pure, it may be recrystallized in a way similar to that just described but with the use of bone-black. It contains one molecule of water of crystallization and has a melting point of 190–192° (cor.). The yield is 420–460 g. (85–91 per cent of the theoretical amount).

The 420–460 g. of crude nicotinic acid nitrate from two runs (not necessarily dry) is dissolved in 900 cc. of boiling water in a 3-l. beaker and 800 g. of crystalline disodium phosphate ($Na_2HPO_4 \cdot 12H_2O$) added with constant stirring. The resulting thick mixture is stirred and heated almost to boiling for five minutes and then allowed to cool. The mixture is finally chilled to 0° by an ice bath. It is well to stir occasionally during the crystallization to prevent the formation of too solid a cake of crystalline material. The nicotinic acid is filtered off upon a 15-cm. Büchner funnel and washed with three 100-cc. portions of cold water.

The yield is 260–300 g. of material containing a small amount of mineral salts but otherwise nearly pure. It can be purified further by recrystallization from 2.5 to 3.5 l. (Note 4) of hot water, 150–180 g. of material, which melts at 230–232° (cor.), being obtained. The yield of recrystallized material is 50–60 per cent of the theoretical amount, based upon the nicotine employed.

The recrystallization is the least satisfactory part of this procedure and involves the greatest apparent loss of material; the product before recrystallization is sufficiently pure for most purposes. By evaporation of the mother liquors, 40–45 g. of pure nicotinic acid may be obtained, making the total yield of pure material 190–225 g. (63–74 per cent of the theoretical amount); in addition, a small amount of somewhat less pure material is recovered.

## 2. Notes

1. Fuming nitric acid, the use of which is advised in the literature, is not as convenient to use and gives no better results than concentrated nitric acid.

2. A product of 100 per cent purity gives no better results

than does the crude 95 per cent material used in this experiment. The nicotine was purchased from the Hall Tobacco Company, of St. Louis, Mo.

3. If the nicotine and nitric acid mixture is merely placed on a steam bath and allowed to heat without control of the temperature, an occasional run will react violently, with loss of material.

4. The amounts of solvent given for the various recrystallizations are those which give best yields and it is advisable to follow them as closely as possible.

5. Nicotinic acid hydrochloride may be obtained directly from the nitrate by heating on a steam bath 460 g. of crude nitrate with 1000 cc. of concentrated hydrochloric acid (sp. gr. 1.19). After six to eight hours, the evolution of gas ceases and the liquid is evaporated under diminished pressure. The dry salt is again treated with 500 cc. of hydrochloric acid and heated for five hours and then evaporated as before.

After the salt has been again obtained, it is dissolved in 400 cc. of hot water and the solution diluted with four times its volume of 95 per cent alcohol. Upon cooling and stirring, the hydrochloride, melting at 273–274°, is obtained in a yield of 245–250 g. An additional quantity of 75–80 g. may be obtained from the mother liquors.

### 3. Other Methods of Preparation

Nicotinic acid has been prepared by the oxidation of nicotine with nitric acid.[1] It has also been prepared by the action of potassium permanganate upon β-picoline, nicotine, lutidine, β-phenyl pyridine, and β-dipyridyl[2] and by the action of chromic acid upon nicotine and β-phenyl pyridinecarboxylic acid.[3]

It may also be obtained by heating quinolinic acid[3] and certain other pyridine dicarboxylic acids.[2] The nitrile has been prepared by heating sodium β-pyridinesulfonate with potassium cyanide.[4]

[1] Ann. **165**, 330 (1873); Ber. **34**, 702 (1901); Chem. Zentr. **1898** (I), 677.

[2] Beilstein **4**, 143 (1899); **4***, 108 (1906).

[3] Rec. trav. chim. **1**, 121 (1882); Arch. Pharm. **240**, 353 (1902).

[4] Ber. **15**, 63 (1882).

# PENTAERYTHRITOL

## (Tetra-hydroxymethyl methane)

$$8CH_2O + 2CH_3CHO + Ca(OH)_2 \rightarrow 2C(CH_2OH)_4 + (HCO_2)_2Ca$$

Prepared by CHEMICAL LABORATORY, PICATINNY ARSENAL.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

IN a 6-gal. crock provided with an efficient stirrer are placed 10.5 l. of water, 5600 g. commercial (35–40 per cent) formaldehyde, and 630 g. of acetaldehyde (b.p. 20–22°). To this mixture is added, during the course of one-half hour, with constant mechanical stirring, 475 g. of high-grade quicklime to which enough water has been added to cause the disintegration of lumps by slaking. This lime must be in the form of a fine powder (Note 1). During the addition, the temperature of the mixture is raised by injection of live steam (Note 2) to 60–65°, and is held at this point for two hours after all has been added (Note 3).

The mixture is then cooled by surrounding the crock with cold water, and about 1700 g. of cold 50 per cent sulfuric acid is added, until a filtered sample just fails to yield a further precipitate of calcium sulfate upon the further addition of sulfuric acid. The calcium sulfate is filtered off and washed with cold water. A saturated aqueous solution of oxalic acid is cautiously added to the filtrate until a filtered sample gives no test for calcium salts in solution (Note 4).

The resulting solution, which should now be clear and lemon yellow in color (Note 5), is concentrated under reduced pressure on the steam bath (Note 6, Fig. 3) until the volume is reduced

to 3.5–4 l. It is then cooled and the crystalline precipitate filtered off by suction and washed with methyl alcohol or 95 per cent ethyl alcohol (Note 7) in small portions, until the washings are colorless. The product thus obtained weighs 900–960 g. and melts without decomposition at 250–252° (Note 8). The mother liquor and washings are further concentrated (Note 9) to a syrup, from which a second crop of 100–250 g. is obtained upon cooling. This is washed as before with alcohol but pos-

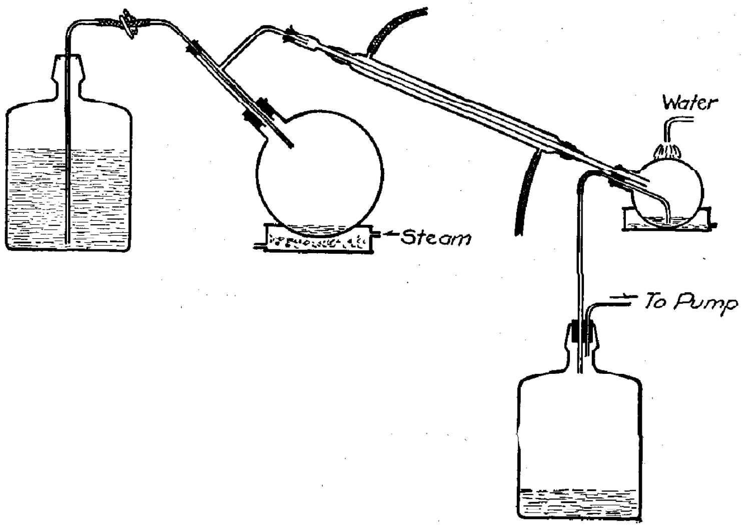



FIG. 3.

sesses a slightly yellow color and must be recrystallized from an equal weight of water. The total yield of product of m.p. 250–252° is 975–1055 g. (50–54 per cent of the theoretical amount).

## 2. Notes

1. The quicklime may be ground mechanically before addition, but this is less convenient than disintegrating it by the cautious addition of water.

2. If mechanically powdered quicklime is used, the use of steam is unnecessary, and the temperature is to be controlled

by the rate of addition. The use of heating and cooling coils in the crock is most convenient if available; such coils may safely be of iron tubing. Temperatures above 65° result in a lower yield of less pure product.

3. After the mixture has been maintained at 60–65° for a period of about one hour, the initial gray color undergoes a rapid change to yellow. This change is accompanied by a marked diminution in the odor of aldehydes.

4. The presence of only a slight excess of oxalic acid is permissible, although it is essential to remove all calcium salts since they would contaminate the final product; but small quantities of free oxalic acid do not interfere with the subsequent operations and are removed in the mother liquors.

5. The liquor may profitably be treated with decolorizing carbon at this point.

6. The apparatus shown in Fig. 3 has been found convenient for such evaporations under reduced pressure. The distillation is started with 3.5–4 l. in the 12-l. flask, and the level of liquid is maintained by controlling the rate of addition by means of a screw clamp. A 2-l. flask has been found satisfactory for the condensing intermediate receiver, provided the outside be completely wetted by the cold water.

7. Nearly 1 l. of ethyl alcohol is required. Pentaerythritol is insoluble in the cold alcohol, which dissolves the sticky polymerized aldehydes obtained on concentrating the solution.

8. The product is sufficiently pure for most purposes, but may be recrystallized from slightly more than an equal weight of boiling water.

9. The washings may be collected separately and the alcohol recovered by distillation from a steam bath under slightly reduced pressure.

### 3. Other Methods of Preparation

The only practicable process for the preparation of pentaerythritol consists in condensing acetaldehyde with formaldehyde in dilute aqueous solution by means of calcium (or barium)

hydroxide;[1] it has, however, also been formed by the action of sodium amalgam upon the pentaerythrose produced by condensing acetaldehyde with formaldehyde by means of sodium hydroxide.[2]

[1] Ann. **265**, 316 (1891); Ann. **276**, 58 (1893); C. A. **11**, 2543 (1917); D. R. P. 390,622; Chem. Zentr. **1924** (1) 2396.

[2] Am. Chem. J. **37**, 38 (1907).

# XXI

## β-PHENYLHYDROXYLAMINE

$$C_6H_5NO_2 + 2Zn + H_2O \rightarrow C_6H_5NHOH + 2ZnO$$

Prepared by OLIVER KAMM.
Checked by C. S. MARVEL.

### 1. Procedure

IN a 4-gal. earthenware jar are placed 250 g. of technical ammonium chloride, 8 l. of water, and 500 g. of nitrobenzene. The mixture is stirred vigorously by means of a mechanical stirrer, and 620 g. of zinc dust of 85 per cent purity is added (Note 1) during the course of fifteen to twenty minutes (Note 2). As the reduction proceeds, the temperature rises to 60–65°. Stirring is continued for fifteen minutes after all the zinc dust has been added, at the end of which time the reaction is complete, as indicated by the fact that the temperature of the mixture ceases to rise.

While still hot, the solution is filtered with suction in order to remove the zinc oxide, which is washed with 1 l. of hot water. The filtrate is placed in an enamelled pan, saturated with salt, about 3 kg. being required, and cooled to 0° by being placed in an ice-salt mixture. The phenylhydroxylamine, which crystallizes out in long, light yellow needles (Note 3), is filtered by suction. The yield of crude product varies considerably, depending upon the amount of salt solution present, but averages 350–400 g. This corresponds to 275–300 g. (62–67 per cent of the theoretical amount) of actual phenylhydroxylamine, as determined by its separation from inorganic materials by solution in ether (Note 4).

Since phenylhydroxylamine deteriorates upon storage, it is generally used promptly, as illustrated in the preparation of cupferron, p. 19. The oxalate is somewhat more stable.

## 2. Notes

1. The zinc dust must be analyzed (Gattermann, "Practical Methods of Organic Chemistry," 3rd ed., p. 390), and a proportional quantity used if the zinc content is not 85 per cent. Technical nitrobenzene is satisfactory if it distils over a range of not more than 5 degrees and is not acid in reaction.

2. When the reaction is run more slowly, the temperature does not reach 60–65° and the yield is poorer. At 50–55°, the yield is about 55 per cent.

3. It is important that the phenylhydroxylamine solution be kept at 0° for at least one-half hour or considerable material will be lost in the solution. The use of an enamelled pail saves a great deal of time at this step.

4. Phenylhydroxylamine is soluble in saturated salt solution at 0° to the extent of about 9 grams per liter, but this amount is not included in the yields given. Occasional yields of 300–310 g. of dry phenylhydroxylamine have been obtained.

## 3. Other Methods of Preparation

Although phenylhydroxylamine may be prepared by catalytic reduction,[1] by the oxidation of aniline,[2] and by electrolytic reduction of nitrobenzene,[3] the most feasible method is still based upon the original zinc reduction method of Bamberger [4] and of Wohl.[5] Various solvents and catalysts have been used in this reduction, and copper-coated and amalgamated zinc, as well as aluminium amalgam,[6] have been substituted for zinc dust. The method herein recommended is essentially one previously described [7] but it has been found [8] that cooling is not an essential, as claimed in the patents. The preparation of the oxalate is also a more recent contribution.[9]

[1] Ber. **55B**, 875 (1922). [2] Ber. **32**, 1676 (1899).

[3] Chem. Zentr. **1898** (II), 634; Z. physik. Chem. **32**, 272 (1900); J. Phys. Chem. **19**, 696 (1915).

[4] Ber. **27**, 1348, 1548 (1894). [5] Ber. **27**, 1432 (1894).

[6] Beilstein **2***, 241 (1903); J. Chem. Soc. **119**, 767 (1921); J. Ind. Eng. Chem. **12**, 799 (1920).

[7] D. R. P. 89,978; Frdl. **4**, 47 (1896). [8] J. Am. Chem. Soc. **41**, 277 (1919).

[9] U. S. Patent 1,390,260; C. A. **16**, 105 (1922).

# XXII

## *n*-PROPYLBENZENE

$$C_6H_5CH_2Cl + Mg \rightarrow C_6H_5CH_2MgCl$$

$$C_6H_5CH_2MgCl + (C_2H_5)_2SO_4 \rightarrow C_6H_5CH_2CH_2CH_3 + MgCl(SO_4C_2H_5)$$

Prepared by HENRY GILMAN and C. H. MEYERS.
Checked by C. S. MARVEL and H. O. CALVERY.

### 1. Procedure

IN a 5-l. flask standing in an empty water bath are placed 50 g. of clean magnesium turnings and 600 cc. of dry ether which has been distilled over phosphorus pentoxide and stored over sodium; the flask is then fitted with a stirrer having a mercury seal, a thermometer, an efficient reflux condenser, and a dropping funnel. About 50 cc. of a solution of 253 g. of benzyl chloride, boiling at 172–175°, in 800 cc. of dry ether is then added through the dropping funnel and the mixture heated just to boiling by placing in the bath enough water at 40° to cover about half the surface of that part of the flask which is in contact with the ethereal mixture.

As soon as the ether begins to boil, the warm water is siphoned out; if the boiling should continue vigorously, owing to the reaction having set in, the rate may be regulated by placing cold water in the bath. The remainder of the benzyl chloride solution is then added at such a rate that the mixture boils gently; this will require about four hours. When all has been added, stirring is commenced and the mixture gently boiled for fifteen minutes by the gradual replacement of the cold water by warm.

The temperature of the mixture is then lowered by means of running water, and 385 g. of C. P. ethyl sulfate (Note 1) is dropped in, with continuous stirring, during one and a half hours, allowing the temperature to rise gradually. When all has been added, stirring is continued with gentle boiling for an hour. The cooled mixture is then poured cautiously, with stirring, upon a mixture of 1 kg. of crushed ice, 1 kg. of water, and 200 cc. of concentrated hydrochloric acid.

After a few minutes, the bulk of the water layer is removed by a siphon and the clear ethereal solution decanted, so far as possible, into a 2-l. flask. The remaining mixture is filtered through a glass-wool plug into a separatory funnel, and after removal of the aqueous portion, the remaining ethereal solution is added to that in the flask. An efficient fractionating column is attached, and the ether distilled on the water bath; the residue is then fractionated and collected as pure *n*-propylbenzene boiling at 154–158°. The yield is 133–156 g. (55–65 per cent of the theoretical amount).

## 2. Notes

1. The technical grade of diethyl sulfate gives poorer yields on account of the presence of free acid. The C. P. grade was used in order to obtain the results given in the procedure.

## 3. Other Methods of Preparation

*n*-Propylbenzene has been prepared by the action of sodium on a mixture of propyl bromide and bromobenzene,[1] of zinc dust upon a benzene solution of allyl bromide,[2] and of zinc ethyl upon benzyl chloride;[3] and aluminium chloride has been employed to condense benzene with propyl bromide,[4] allyl

[1] Ann. **149**, 324 (1869).
[2] Jahresb. **1895**, 1516; Bull. soc. chim. (3) **16**, 126 (1896).
[3] Ber. **10**, 294 (1877); Gazz. chim. ital. **7**, 21 (1877).
[4] Ber. **24**, 768 (1891); J. Russ. Phys. Chem. Soc. **27**, 457 (1895); Bull. soc. chim. (3) **16**, 864 (1896).

chloride [5] and trimethylene bromide,[6] but the tendency of this reagent to induce isomerization is a distinct danger.

*n*-Propylbenzene has also been obtained by the action of hot sulfuric acid upon a mixture of propyl alcohol and benzene.[7] Reduction methods have been applied to various monosubstituted benzene derivatives possessing a three-carbon-chain, namely, phenyl ethyl ketone and benzyl methyl ketone,[8] $\gamma$-phenyl *n*-propyl chloride or bromide,[9] propenylbenzene,[10] phenyl ethyl ketoxime [11] and cinnamyl alcohol or phenyl allyl alcohol.[12]

[5] Ann. **218**, 379 (1883); Bull. soc. chim. (2) **41**, 197 (1884); (2) **43**, 588 (1885).
[6] Compt. rend. **132**, 155 (1901).
[7] Compt. rend. **117**, 236 (1893).
[8] J. prakt. Chem. (2) **81**, 387 (1910); Ber. **46**, 1839 (1913).
[9] Ber. **43**, 178 (1910); **44**, 2872 (1911); **45**, 2176, 2179 (1912).
[10] Ber. **36**, 622, 773 (1903).
[11] Bull. soc. chim. (4) **9**, 465 (1911).
[12] Ber. **39**, 2590 (1906).

# XXIII

# PYRUVIC ACID

$$\begin{array}{l} CHOHCO_2H \\ | \\ CHOHCO_2H \end{array} + (KHSO_4) \rightarrow CH_3COCO_2H + H_2O + CO_2$$

Prepared by J. W. Howard and W. A. Fraser.
Checked by C. S. Marvel and R. L. Shriner.

## 1. Procedure

An intimate mixture of 600 g. of finely powdered freshly *fused* potassium acid sulfate and 400 g. of powdered tartaric acid, prepared by grinding them together in a mortar, is placed in a 3-l. round-bottom Pyrex flask connected with a condenser which is filled with water but does not have any water flowing through it. The mixture is heated by means of an oil bath maintained at a temperature between 210 and 220° until liquid no longer distils over. Some foaming takes place (Note 1), but if fused potassium acid sulfate is used and the temperature of the bath does not rise above 220°, it is not difficult to control. The distillate is then fractionated under reduced pressure. Pyruvic acid passes over at 75–80°/25 mm. and the yield is 117–128 g. (50–55 per cent of the theoretical amount).

## 2. Notes

1. If the mixture foams badly, it may be kept from frothing over by heating the upper part of the flask with a free flame.

2. The cake left in the reaction flask may be removed readily by inverting over a steam jet.

## 3. Other Methods of Preparation

Pyruvic acid has been prepared from $\alpha,\alpha$-dichloropropionic acid and from the corresponding dibromo acid, by heating with

water under pressure, by heating with barium hydroxide solution, and by the treatment of the aqueous solutions with silver oxide or silver carbonate.[1] The action of sodium hydroxide on $\alpha,\alpha$-dibromopropionic acid has also been studied.[2] Better results have been reported from the hydrolysis of acetyl cyanide and of oxalacetic ester.[3]

It has been obtained by the oxidation of lactic acid,[4] mesaconic acid and citraconic acid,[5] acetone and acetol,[6] but in general these oxidation procedures are not suitable as preparative methods.

Pyruvic acid may be obtained by the distillation of tartaric acid or glyceric acid.[7] Better results are obtained, however, by the distillation of tartaric acid in the presence of a dehydrating agent such as potassium bisulfate.[8] This method has been adopted after a study of a variety of dehydrating agents and various experimental procedures.

[1] Ber. **5**, 477 (1872); **10**, 264, 2037 (1877); **18**, 228, 235 (1885).

[2] Ann. **342**, 132 (1905).

[3] Ber. **11**, 620, 1563 (1878); Ann. **246**, 327 (1888).

[4] J. Chem. Soc. **77**, 71 (1900); Ber. **17**, 840 (1884); Chem. Met. Eng. **28**, 357 (1923).

[5] Ann. **305**, 48, 49 (1899).

[6] Compt. rend. **140**, 1592 (1905); Bull. soc. chim. (4) **3**, 259 (1908); Ber. **20**, 641 (1887); J. Am. Chem. Soc. **39**, 2661 (1917).

[7] Ann. physik. (2) **36**, 1 (1835); Ann. **131**, 338 (1864); **188**, 314 (1877).

[8] Ber. **14**, 321 (1881); Bull. soc. chim. (3) **13**, 335 (1895); Rec. trav. chim. **19**, 278 (1900); Ann. **242**, 269 (1887); Ber. **43**, 2188 (1910).

## XXIV

## SODIUM p-HYDROXYPHENYLARSONATE

$$C_6H_5OH + H_3AsO_4 \rightarrow HOC_6H_4AsO_3H_2 + H_2O$$

Prepared by W. G. CHRISTIANSEN and A. J. NORTON.
Checked by OLIVER KAMM.

### 1. Procedure

SEVEN HUNDRED AND TWENTY grams of syrupy arsenic acid (75–80 per cent) is boiled in a beaker until the temperature of the acid is 150°; about 120 g. of water is driven off, leaving a syrup containing approximately 95 per cent of orthoarsenic acid, which is then added to 300 g. of phenol in a 1-l. round-bottom, short-neck Pyrex flask. By means of a 3-hole stopper, an efficient jacketed stirrer (Org. Syn. **1**, 4) and a thermometer are introduced into the flask, and a connection is established with a downward condenser. The flask is set in an oil bath which is heated at once to 155–160°, and the stirrer is run at a rate high enough to insure thorough mixing.

When the inside temperature reaches 140°, boiling commences and water plus a very little phenol begins to distil. The distillation is allowed to continue until 60 cc. (one molecular equivalent) of water has been collected; this usually requires one hour, and the inside temperature rises to 146°. The downward condenser is then replaced by a reflux condenser (Note 1) and the reaction is allowed to continue until a total of four hours has elapsed from the time the contents of the flask first reached 140°. After the return condenser has been attached, the inside temperature declines slowly to 141° or 142° and the reaction mixture becomes thicker and somewhat tarry. After the contents of the flask have been partially cooled, they are

poured into 4 l. of water and mechanically stirred; the agitation is continued for a short time in order to break up the tarry material and enable the water to dissolve the hydroxyphenylarsonic acids completely.

Finely ground barium hydroxide is added gradually to the well-stirred water solution until the material is slightly alkaline to litmus, in order to remove the excess of arsenic acid; when this point is reached, the solution becomes pink. If the procedure is carried out properly, 700–800 g. of $Ba(OH)_2 \cdot 8H_2O$ should suffice (Note 2). The time required by this method is greater than when a hot solution of barium hydroxide is used, but the method is more convenient and does not cause such a great increase in volume. After removal of the barium arsenate by filtration, the mother liquor and washings are treated with sulfuric acid until the solution contains neither barium nor sulfate ions. When the barium sulfate has been separated and thoroughly washed (Note 3), the filtrate is concentrated on a steam bath to about 3 l., neutralized to litmus with sodium hydroxide, filtered, evaporated until the solution becomes well coated with crystals, and then treated with 2.5 volumes of alcohol. After the mixture has cooled in an ice-box, the sodium *p*-hydroxyphenylarsonate is separated, washed with alcohol, and dried in an oven at 80°. A second crop may be secured from the filtrate by concentrating it further and precipitating with alcohol. The total yield of anhydrous sodium *p*-hydroxyphenylarsonate is 252 g. (33 per cent of the theoretical amount). By proper manipulation, it is possible to obtain as much as 240 g. in the first crop and to have it free from sulfate, arsenate, and sodium *o*-hydroxyphenylarsonate which is one of the by-products formed in this reaction (Note 4).

## 2. Notes

1. When the downward condenser is not replaced by a reflux condenser, the total volume of water that distils is 90–120 cc. and the mass becomes very tarry, owing to the oxidation of phenol or of some intermediate substance formed in the reaction.

*p*-Hydroxyphenylarsonic acid is not destructively oxidized by hot arsenic acid.

2. In removing the excess arsenic acid with barium hydroxide, the solution should not be permitted to become strongly alkaline, as the barium salt of the hydroxyphenylarsonic acid may commence to separate, thereby decreasing the yield.

3. The filtration of large quantities of barium sulfate is usually tedious; but if filtering carbon is added to the suspension to be filtered and if a mat of this carbon is prepared on the filter by filtering an aqueous suspension of carbon, the barium sulfate may be removed rapidly and completely, even when it is precipitated from cold solutions.

4. When phenol is arsonated with arsenic acid, small amounts of *o*-hydroxyphenylarsonic acid, *p,p'*-di-hydroxyphenylarsinic acid and *o,p'*-di-hydroxyphenylarsinic acid are formed as by-products. As the sodium salts of the secondary acids are soluble in alcohol, they will not appear in the material precipitated by the addition of alcohol. The sodium salt of *o*-hydroxyphenylarsonic acid, although insoluble in alcohol, will not be precipitated if the solution is not concentrated too far before addition of the alcohol. To test the material for the presence of the ortho compound, ferric chloride is added to an aqueous solution of a small amount of the solid; the ortho hydroxy acid gives a deep purple color, whereas the para acid gives no coloration. The sodium salt which is precipitated with alcohol contains water of crystallization, which is driven off by drying at 80°. The product can be purified by dissolving in hot water and adding hot alcohol until a slight permanent turbidity is produced. Upon cooling, the material separates in a crystalline condition. Occasionally, the second crops of sodium *p*-hydroxyphenylarsonate contain small amounts of arsenious oxide which is formed from the arsenic acid during the oxidation mentioned above.

### 3. Other Methods of Preparation

*p*-Hydroxyphenylarsonic acid may be prepared by diazotization of arsanilic acid and replacement of the diazo group by

hydroxyl.[1] The method of directly introducing the arsenic acid group into phenol is more satisfactory. This preparation was first described in the patent literature,[2] but the method proved unworkable and was reinvestigated and improved by Conant [3] and later by Jacobs and Heidelberger.[4] In the present method,[5] additional improvements have been effected.

[1] Ber. **41**, 1854 (1908).
[2] D. R. P. 205,616; Frdl. **9**, 1040 (1908).
[3] J. Am. Chem. Soc. **41**, 431 (1919).
[4] J. Am. Chem. Soc. **41**, 1440 (1919).
[5] J. Am. Chem. Soc. **45**, 2188 (1923).

# XXV

## *o*-TOLUNITRILE AND *p*-TOLUNITRILE

$$CH_3C_6H_4NH_2 + HNO_2 + HCl \rightarrow CH_3C_6H_4N_2Cl + 2H_2O$$

$$CH_3C_6H_4N_2Cl + NaOH + NaCu(CN)_2 \rightarrow CH_3C_6H_4CN + N_2 + NaCl + CuCN$$

Prepared by H. T. Clarke and R. R. Read.
Checked by C. S. Marvel and M. M. Brubaker.

### 1. Procedure

A. *Preparation of the cuprous cyanide solution:* Cuprous chloride prepared from 1250 g. of copper sulfate, according to the directions given in Org. Syn. **3**, 33, is suspended in 2 l. of cold water in a 15-l. crock fitted with a mechanical stirrer. A solution of 650 g. of sodium cyanide (96–98 per cent) in 1 l. of water is added and the mixture stirred, whereupon the cuprous chloride enters into solution with considerable evolution of heat (Note 1). The mixture is then cooled by surrounding the crock with cold water (Note 2).

B. *Preparation of o-tolunitrile:* While the cuprous cyanide solution is cooling, 428 g. of *o*-toluidine is mixed in a 20-l. crock with 1 l. of commercial 28 per cent hydrochloric acid (sp. gr. 1.14) and enough cracked ice, about 4 kg., to bring the temperature of the mixture to 0°. A solution of 280 g. of sodium nitrite in 800 cc. of water is added, with stirring, to the resulting suspension of *o*-toluidine hydrochloride, the temperature being kept at 0–5° by the addition of cracked ice. The addition of the nitrite occupies about fifteen minutes; at the end of the operation, the mixture must show a distinct and permanent reaction for free nitrous acid on testing with starch iodide paper (Note 3). The final volume of the solution is 5–6 l. The mixture is now

cautiously neutralized by adding dry sodium carbonate with constant stirring, using litmus paper to determine the end point; about 200 g. of the anhydrous carbonate is required (Note 4).

The cold cuprous cyanide solution is now chilled to 0–5° by the addition of ice, and 1 l. of benzene is poured on the surface. To this mixture is slowly added the cold neutralized diazonium solution. During the addition, which occupies about thirty minutes, such vigorous stirring is maintained that the benzene on the surface is constantly drawn to the stirrer, and the temperature is maintained at 0–5° by occasionally adding ice. As soon as the diazonium solution comes into contact with the cuprous cyanide, a dark yellow, oily precipitate is formed which at once begins to give off nitrogen; the resulting nitrile is taken up by the benzene as soon as it is formed (Note 5). When all has been added, the temperature is held at 0–5° for thirty minutes longer, and then is allowed to rise to that of the room (20–25°), which usually requires about three hours.

After stirring has been continued for two hours longer, the crock is surrounded by hot water or steam and warmed to 50° without stirring. The mixture is then allowed to stand until cool, when the aqueous layer is drawn off by means of a siphon. The upper oily layer is transferred to a 12-l. flask and distilled in a current of steam until no more oil passes over; about 10 l. of distillate is collected (Note 6). The water is drawn off and the benzene removed by distillation, by means of a 2-l. round-bottom flask and a fractionating column about 90 cm. long. When benzene no longer distils over, the distillation is continued in the same apparatus under reduced pressure, and the fraction that boils at 94–96°/20 mm. is collected. A small amount of dark-colored residue remains in the flask. The yield of almost colorless *o*-tolunitrile is 300–330 g. (64–70 per cent of the theoretical amount).

*p*-Tolunitrile can be prepared in exactly the same manner from *p*-toluidine; the product, which distils at 104–106°/20 mm., solidifies in the receiver to a mass of nearly colorless needles which melt at 25–27°. The yield is the same as with the ortho compound (Note 7).

## 2. Notes

1. If desired, the cuprous chloride may be suspended in 3 l. of water and the sodium cyanide added in the solid form.

2. If several runs are to be made it may be more convenient to prepare a large quantity of cuprous cyanide solution, since this appears to be stable for several days.

3. If the sodium nitrite is not of the highest technical purity it may be necessary to employ more than the indicated quantity. It is essential that the test for nitrous acid be permanent; if any unchanged amine remains, a precipitate of the diazoamino compound is formed on neutralization. A moderate excess of nitrite does not appear to interfere with the reaction, especially since the greater portion of the free nitrous acid is removed by the carbon dioxide liberated on neutralization.

4. Sodium carbonate is preferable to sodium hydroxide because very little heat is evolved on neutralization. A slight excess of carbonate does not appear to be harmful.

5. It is essential that the stirring be very vigorous. If the intermediate addition compound is allowed to collect on the surface of the liquid, it decomposes spontaneously with evolution of much heat; this decomposition may take place with almost explosive violence. The presence of the benzene tends to diminish the viscosity of the intermediate product and permit it to be readily distributed throughout the mixture. Decomposition is quite rapid at 0° and is practically complete when room temperature is reached; it appears, however, to be advisable to warm the mixture to 50°, since if this be omitted the yield is slightly decreased.

6. The apparatus described in Org. Syn. **2**, 80, is suitable for the steam distillation.

7. The product, as obtained in the above procedure, is of high purity; cresols do not appear to be formed under the conditions specified. The process has the advantage over that described in the literature [1] of giving rise to no poisonous fumes during the formation of the cuprous cyanide and during the interaction of this with the diazonium salt. The yield is practically the same as in the older method.

### 3. Other Methods of Preparation

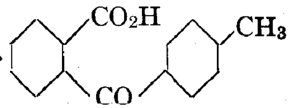
The original method of Sandmeyer [1] prescribed the preparation of the cuprous cyanide solution by dissolving copper sulfate in potassium cyanide solution and adding the strongly acid diazonium solution to it. Both of these operations involve the evolution of poisonous gases—cyanogen in the first case and hydrogen cyanide in the second. Slight modifications have been subsequently suggested: the use of a 50 per cent excess of cuprous cyanide [2] and the heating of the cuprous cyanide solution before the reaction.[3]

*o*-Tolunitrile has also been prepared from *o*-toluidine by conversion into *o*-tolyl isothiocyanate and the boiling of this under a reflux condenser; [4] *p*-tolunitrile has been prepared by distilling *p*-toluic acid with potassium thiocyanate; [5] and a mixture of the two has been produced by the interaction of toluene, mercury fulminate, and aluminium chloride.[6]

[1] Ber. **17**, 2653 (1884); **18**, 1492, 1496 (1885).
[2] Ber. **19**, 756 (1886).
[3] Ber. **23**, 1026 (1890).
[4] Ber. **6**, 419 (1873).
[5] Ber. **8**, 441 (1875).
[6] Ber. **36**, 14 (1903).

# XXVI

## *p*-TOLUYL-*o*-BENZOIC ACID

$C_6H_4(CO)_2O + C_6H_5CH_3\ (Al_2Cl_6) \rightarrow$ 


Prepared by L. F. Fieser.
Checked by Roger Adams and R. L. Shriner.

### 1. Procedure

A 2-l. round-bottom flask is clamped to a ring-stand and equipped with a rubber stopper protected with tin foil and carrying a glass stirrer with mercury seal and a reflux condenser. (Cf. Org. Syn. 1, 4, Fig. 1, *a*.) As an outlet for the hydrogen chloride, the top of the condenser is provided with a bent tube which almost touches the surface of the water in a half-filled 1-l. flask.

One hundred grams of phthalic anhydride and 400 g. of toluene are placed in the flask, which is cooled in an ice bath while 200 g. of anhydrous aluminium chloride (Note 1) is being ground to a fine powder. The chloride is now added all at once, and connections to the condenser made as rapidly as possible. Stirring is commenced at once and the ice bath is removed. The mixture warms up considerably and becomes olive-green in color. When the evolution of hydrogen chloride begins to slacken (ten minutes) a water bath is put into place and heated to 90° in the course of forty-five minutes. The temperature of the bath is kept at 90° and vigorous stirring continued for two and one-half hours. At this point, the evolution of hydrogen chloride will have practically ceased and the reaction will have been completed. The hot water in the bath is replaced first by cold water and then by ice, while stirring is continued.

As soon as the flask is well cooled, it is disconnected and carried to the hood, and ice is slowly added, with shaking, until the dark mass is completely decomposed and the flask is about half filled with the mixture. After 150 cc. of crude concentrated hydrochloric acid has been added, the mass coagulates and the solution clears; the flask is then heated on the steam bath while preparations are being made for steam distillation.

This operation, which removes the excess of toluene, may be carried out in the same flask and loss by transfer thus avoided (Note 2). The aqueous solution of aluminium chloride and hydrochloric acid, after thorough cooling, is decanted through a suction filter, the residue washed with a little cold water, and that collected on the filter returned to the flask. This residue consists almost solely of toluylbenzoic acid, partly crystalline, partly in oily lumps.

A previously prepared and heated solution of 50 g. of sodium carbonate in 1 l. of water is added, and steam is passed in to provide heat and agitation. With a rapid stream, the acid will go into solution in about ten minutes, leaving a small amount of brown, tarry material and a little alumina undissolved (Note 3). The solution is filtered while hot and transferred to a 2-l. beaker, and the acid precipitated by the addition of 65 cc. of concentrated hydrochloric acid. The acid separates as an oil, which soon crystallizes. The solution is cooled in ice and the acid filtered and washed.

The air-dried product is pure white and weighs 170 g. (Note 4). After drying at 100°, the anhydrous acid melts at 138–139° and weighs 157 g. (96 per cent of the theoretical amount). Air-dried material is suitable for the condensation to $\beta$-methyl anthraquinone, p. 43. It may be recrystallized from toluene.

## 2. Notes

1. Although statements are found in the literature that quantitative yields may be obtained with smaller quantities of aluminium chloride, the ratio $1C_6H_4(CO)_2O : 1Al_2Cl_6$ is essential.

2. The steam distillation requires about fifteen minutes, and about 340–380 cc. of toluene is recovered.

3. If, in extracting the acid with sodium carbonate, more than 2–3 g. of material remains undissolved, the residue is treated with dilute hydrochloric acid to remove alumina, washed, and again extracted with a little carbonate solution. This extract is neutralized separately since some tar may separate with the toluyl benzoic acid. In this event, it is filtered and extracted with *cold* carbonate solution, in which the tar is completely insoluble.

4. According to Limpricht, the acid may crystallize either in hydrated or in the anhydrous condition, but the transition temperature is not stated. The loss of water upon drying at $100^\circ$ shows the compound obtained in this experiment to be the monohydrate.

## 3. Other Methods of Preparation

The only practical method for the preparation of *p*-toluyl-*o*-benzoic acid is that proposed by Friedel and Crafts.[1] Limpricht[2] has proposed a decrease in the quantity of aluminium chloride, but Heller and Schulke[3] and McMullen[4] have verified the importance of an excess of the condensing agent.

[1] Ann. chim. phys. (6) **14**, 447 (1888).
[2] Ann. **299**, 300 (1898).
[3] Ber. **41**, 3632 (1908).
[4] J. Am. Chem. Soc. **43**, 1965 (1921).

## XXVII

## TRICARBALLYLIC ACID

$$CH(CO_2C_2H_5)_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5 + 4H_2O + (HCl) \rightarrow$$
$$CH_2(CO_2H)CH(CO_2H)CH_2CO_2H + CO_2 + 4C_2H_5OH$$

Prepared by H. T. Clarke and T. F. Murray.
Checked by C. S. Marvel and M. M. Brubaker.

### 1. Procedure

In a 3-l. flask, fitted with a stirrer and a fractionating column with condenser for downward distillation, are placed 912 g. of ethyl propane-1,1,2,3-tetracarboxylate (p. 29) and 950 cc. of a solution of equal volumes of pure concentrated hydrochloric acid and distilled water. A receiver with a side-tube is attached to the condenser; this side-tube leads to a water trap. The mixture is boiled, with continual stirring, at such a rate that the alcohol is removed as fast as it is formed, but without undue removal of water from the flask (Note 1). The progress of the reaction can be followed by noting the rate at which carbon dioxide passes through the trap. When the temperature at the head of the column approaches 100°, the flame is turned down so that very little liquid distils over. Heating is continued until evolution of carbon dioxide ceases (Note 2).

The flask is now disconnected from the stirrer and column, and the contents distilled off as completely as possible on the steam bath under reduced pressure. The remaining solid is freed from residual moisture and hydrochloric acid by allowing a slow current of dry air to pass over it, while still heating on the steam bath and maintaining a partial vacuum (Note 3). It is then redissolved in distilled water, and the solution filtered with

the use of decolorizing carbon, and again evaporated under reduced pressure.

The residue, when completely dry, is ground up, mixed to a paste with dry ether, filtered by suction, washed with dry ether and dried. The product so obtained (Note 4) is practically pure and melts at 160–161°. The yield is 474–479 g. (95–96 per cent of the theoretical amount).

## 2. Notes

1. The temperature at the head of the column will give some idea of the relative amount of water passing over with the alcohol, but allowance must be made for the lowering of the distilling temperature by the carbon dioxide evolved.

2. Twelve hours' heating is necessary to complete the reaction.

3. The dry air is best introduced through a tube leading to the bottom of the flask; it is well not to disconnect the condenser, but to note the point at which no more drops condense. The current of dry air should be quite slow—not more than two bubbles per second in the sulfuric acid wash bottle.

4. Tricarballylic acid is readily soluble in water (requiring about twice its weight at room temperature), but may, if desired, be recrystallized from it. Dry ether may also be employed, about 50 parts by weight being necessary.

## 3. Other Methods of Preparation

Tricarballylic acid was originally prepared by hydrolysis of the nitrile obtained from glycerol tribromohydrin and potassium cyanide;[1] it has also been obtained by the reduction of aconitic acid by sodium amalgam[2] or electrolytically.[3] The hydrolysis of ethyl propanetetracarboxylate may be carried out either in acid solution (with hydrochloric acid)[4] or in alkaline solution,[5]

[1] Proc. Roy. Soc. **12**, 237 (1862); Ann. **128**, 352 (1863); Ann. **136**, 272 (1865).
[2] Ann. **132**, 62 (1864); Ber. **22**, 2920 (1889); Ann. **314**, 15 (1901).
[3] Compt. rend. **136**, 1331 (1903).
[4] Ber. **24**, 2889 (1891); Ann. **341**, 102 (1905).
[5] Ber. **23**, 3760 (1890); J. prakt. Chem. (2) **45**, 56 (1892).

the former being the more convenient. Tricarballylic acid is also formed by the acid hydrolysis of the less accessible methyl propanepentacarboxylate [6] and methyl propanehexacarboxylate,[7] as well as by the alkaline hydrolysis of acetyl tricarballylic ester.[8] Finally, it has been obtained by the oxidation of diallylacetic ester with nitric acid [9] and of gallic acid with potassium chlorate and hydrochloric acid.[10]

[6] Ber. **29**, 1742 (1896); Ann. **347**, 7 (1906).

[7] Ber. **29**, 1279 (1896).

[8] Ann. **190**, 324 (1878); Ber. **23**, 3756 (1890).

[9] Ann. **201**, 53 (1880).

[10] Ann. **177**, 292 (1875).

# XXVIII

## TRIPHENYLMETHANE

$$3C_6H_6 + CCl_4 + AlCl_3 \rightarrow (C_6H_5)_3CCl \cdot AlCl_3 + 3HCl$$

$$(C_6H_5)_3CCl \cdot AlCl_3 + (C_2H_5)_2O \rightarrow (C_6H_5)_3CH + CH_3CHO + C_2H_5Cl + AlCl_3$$

Prepared by J. F. NORRIS.
Checked by H. T. CLARKE and T. F. MURRAY.

### 1. Procedure

To a mixture of 292 g. of dry benzene and 116 g. of dry carbon tetrachloride, (Note 1) in a 1-l. flask provided with a reflux condenser having a calcium chloride tube at its upper end, is added 100 g. of anhydrous aluminium chloride in lumps (Note 2). The flask is at once immersed in ice-water to within 5 cm. of the top, and allowed to stand for twenty-four hours, the temperature of the water being allowed to rise to that of the room (Note 3). One hundred and ten grams of anhydrous ether is added in small portions, through the condenser, the flask being shaken occasionally during twenty minutes. The mixture is allowed to stand for twenty-four hours, and is then poured into a 5-l. flask containing 650 g. of ice and 25 cc. of concentrated hydrochloric acid. One liter of benzene is then added, and the mixture heated on a steam bath under a return condenser. After gently boiling for five to ten minutes, the mixture is allowed to cool to 40–50°, when the benzene layer is separated, washed with 700 cc. of warm water containing 25 cc. of concentrated hydrochloric acid, and distilled. After the benzene has been removed under atmospheric pressure, the residue is transferred to a 300-cc. flask and distilled under reduced pressure, and a

fraction boiling over the range 190–215°/10 mm. collected (Note 4). This weighs 135–160 g.; it solidifies on cooling. It is recrystallized from 550–650 cc. of ethyl alcohol (Note 5), and a colorless product, crystallizing in needles which melt sharply at 92°, is obtained. This is filtered off and washed twice with 30-cc. portions of fresh alcohol. The alcoholic mother liquor is concentrated and the residue distilled under reduced pressure, material which distils over at 190–200°/10 mm. being collected. This is recrystallized from ethyl alcohol, and 6–7 g. more of pure material is thus obtained. The total yield is 125–154 g. (68–84 per cent of the theoretical amount).

## 2. Notes

1. A convenient method for removing moisture from the carbon tetrachloride and the benzene consists in distilling off about one-tenth of the liquid; this first fraction contains all the moisture which may have been dissolved in the commercial products. It is, as a rule, unnecessary to distil the remaining liquid before use.

2. The aluminium chloride may be a good grade of technical anhydrous material. If a powdered product be employed, the reaction is apt to proceed too rapidly. The lump material appears to be somewhat more efficient.

3. With shorter periods of standing and lower temperatures, the yield falls off materially. Thus in one experiment in which the mixture was allowed to stand for twenty-four hours at 5–8°, a large proportion of a lower-boiling product (apparently diphenylmethane) was formed, and only 109 g. of crude triphenylmethane was obtained.

4. A dark, tarry residue amounting to 25–40 g. remains in the flask.

5. Methyl alcohol may also be employed, but it is necessary to use 1600–1700 cc. of it. Triphenylmethane dissolves in one-third of its weight of warm benzene; it separates from this solution with benzene of crystallization, which is lost on exposure to air or recrystallization from alcohol.

## 3. Other Methods of Preparation

The process here described consists essentially in the formation of triphenylchloromethane by the interaction of carbon tetrachloride and benzene in the presence of aluminium chloride, and the reduction of this product by ether under the influence of the aluminium chloride present.

Triphenylchloromethane is most satisfactorily prepared by the above method,[1] though ferric chloride may also be employed as a catalyst.[2] Its reduction by means of ether was first observed by Gomberg,[3] the catalyst in this case being zinc chloride; it had previously been shown [4] that triphenylchloromethane (or triphenylcarbinol) is reduced to triphenylmethane by means of alcohol in the presence of sulfuric acid.

Triphenylmethane has hitherto usually been prepared by the interaction of benzene and chloroform in the presence of aluminium chloride [5] or ferric chloride,[2] but the yields are considerably lower. Other methods consist in the action of benzal chloride upon benzene and aluminium chloride,[6] in heating benzal chloride and mercury diphenyl,[7] and in heating a mixture of benzaldehyde, benzene, and zinc chloride.[8]

[1] Ber. **33**, 3147 (1900).

[2] Ber. **32**, 2422 (1899).

[3] J. Amer. Chem. Soc. **35**, 204 (1913).

[4] Ber. **45**, 3188 (1912).

[5] Ber. **14**, 1516 (1881); **26**, 1961 (1893); Bull. soc. chim. (2) **37**, 6 (1882); Ann. **227**, 108 (1885).

[6] Am. Chem. J. **13**, 556 (1891).

[7] Ber. **5**, 906 (1872).

[8] Ann. **242**, 329 (1887).

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# ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS




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# PREFACE TO VOLUME V

THE general plan of this series has been made clear in the earlier volumes. In this volume twenty-four of the thirty-three preparations have been submitted by eighteen contributors, thus showing a cooperation of organic chemists both in this country and abroad which is greatly appreciated by the editors.

Directions are included for the isolation of two amino acids from natural products and it is hoped that other preparations of this type will appear in future volumes.

In accordance with the general policy of including any improved directions for methods included in the previous volumes, a new set of directions for the preparation of ethyl oxalate is given in this volume.

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# ORGANIC SYNTHESES

## I

### *p*-ACETAMINOBENZENE SULFINIC ACID

$$(p)\ CH_3CONHC_6H_4SO_2Cl + Na_2SO_3 + H_2O \rightarrow$$
$$(p)\ CH_3CONHC_6H_4SO_2H + NaCl + NaHSO_4$$

Submitted by S. SMILES and C. M. BERE.
Checked by HENRY GILMAN and F. SCHULZE.

#### 1. Procedure

THE crude *p*-acetaminobenzene sulfonyl chloride (p. 3) obtained from 67.5 g. (0.5 mole) of acetanilide is shaken for two hours with a solution of 250 g. (1 mole) of crystallized sodium sulfite ($Na_2SO_3 \cdot 7H_2O$) in 500 cc. of water. The reaction mixture is kept slightly alkaline by the addition at intervals of small portions of 50 per cent sodium hydroxide solution. The total volume of alkali used varies from 10 to 50 cc. After the alkaline mixture has been shaken for the two-hour period (Note 1) it is filtered, and the filtrate is acidified with 60 per cent sulfuric acid. If the acid is added slowly, the sulfinic acid comes down in fine crystals which after filtering and drying, melt at 155° with decomposition (Note 2). The yield is 50–55 g. (43–47 per cent of the theoretical amount based on the acetanilide used).

The product may be purified by crystallization from 400 cc. of hot water, but this is unnecessary when the above procedure is followed carefully.

## 2. Notes

1. The solution does not clear up when reduction is complete on account of the formation of a gelatinous impurity. Two hours suffice for the completion of reduction.

2. The melting point given in the literature (180°) is incorrect, its publication being due to a typographical error. The observed melting point varies slightly with the rate of heating during the determination of the melting point.

## 3. Other Methods of Preparation

*p*-Acetaminobenzene sulfinic acid has been prepared only by the reduction of *p*-acetaminobenzene sulfonyl chloride.[1]

[1] J. Chem. Soc. **125**, 2361 (1924).

# II

## *p*-ACETAMINOBENZENE SULFONYL CHLORIDE

$$C_6H_5NHCOCH_3 + 2HOSO_2Cl \rightarrow$$
$$(p)\ CH_3CONHC_6H_4SO_2Cl + HCl + H_2SO_4$$

Submitted by S. Smiles and Jessie Stewart.
Checked by Henry Gilman and F. Schulze.

### 1. Procedure

In a 500 cc. round-bottom flask, fitted with a mechanical stirrer, is placed 290 g. (2.49 moles) of chlorosulfonic acid (Note 1). The flask is surrounded by a cooling bath and cooled with running water to about 12–15°. To the chlorosulfonic acid is added gradually 67.5 g. (0.5 moles) of acetanilide. This requires about fifteen minutes if the temperature is maintained at approximately 15°. Since large volumes of hydrogen chloride are evolved, the reaction should be conducted in a good hood. After all of the acetanilide has been added, the mixture is heated to 60° for two hours to complete the reaction (Note 2).

The syrupy liquid is poured slowly, with stirring (Note 3), into 1 kg. of ice to which just enough water has been added to make stirring easy. This decomposition of the excess chlorosulfonic acid should be carried out in the hood. The solid sulfonyl chloride which separates is collected on a suction funnel (Note 4) and washed with water. The yield of crude material is 90–95 g. (77–81 per cent of the theoretical amount based on the acetanilide).

This crude material may be used directly in many preparations such as *p*-acetaminobenzene sulfinic acid (p. 1). If a pure product is desired, the crude material is dried by pressing on a porous plate and then crystallized from dry benzene. The acid

chloride is slightly soluble in benzene and only 1.5 to 2 g. will dissolve in 100 cc. of hot benzene. On cooling, about 75 per cent of the material separates from the benzene in thick, colorless prisms melting at 149° (Note 5).

## 2. Notes

1. The chlorosulfonic acid should be freshly distilled. Smaller amounts of this reagent may be used without reducing the yield or affecting the quality of the product. However, with smaller amounts the time required for the reaction must be increased. Thus, if 175 g. of chlorosulfonic acid is used with 67.5 g. of acetanilide, an additional hour of heating is required to obtain the yields mentioned above.

2. The hydrogen chloride which is liberated during the reaction fills the mixture with tiny bubbles. When these disappear the reaction is complete.

3. Mechanical stirring is most convenient but not necessary.

4. A rather large suction funnel (125 mm. or more) should be used in the filtration as the sulfonyl chloride has a tendency to clog the filter.

5. The purification is the least satisfactory part of the preparation. The material must not be heated while water is still present, or excessive decomposition will occur. As the sulfonyl chloride is only slightly soluble in hot benzene, it is inconvenient to crystallize more than a small amount at a time. The crude product does not keep well and must be used at once. After recrystallization it may be kept indefinitely.

## 3. Other Methods of Preparation

*p*-Acetaminobenzene sulfonyl chloride has been prepared by the action of phosphorus pentachloride on sodium *p*-acetaminobenzene sulfonate[1] and by the action of chlorosulfonic acid on acetanilide.[2]

[1] Ber. **39**, 1563 (1906).
[2] J. Chem. Soc. **121**, 2558 (1922).

## III

## ACETONE DICARBOXYLIC ACID

$$CO_2HCH_2C(OH)(CO_2H)CH_2CO_2H + (\text{fuming } H_2SO_4) \rightarrow CO_2HCH_2COCH_2CO_2H + H_2O + CO$$

Submitted by Roger Adams, H. M. Chiles, and C. F. Rassweiler.
Checked by H. T. Clarke and T. F. Murray.

### 1. Procedure

In a 5-l. round-bottom flask (Note 1), fitted with an efficient mechanical stirrer, is placed 3000 g. of fuming sulfuric acid (20 per cent of free sulfur trioxide). Then the flask is cooled very efficiently with a thick pack of ice and salt, until the temperature of the acid registers $-5°$ (Note 2). The stirring is started, and 700 g. of finely powdered U. S. P. citric acid is added gradually. The speed of the addition is regulated according to the temperature of the reaction mixture. The temperature should not rise above 0° until half of the citric acid has been added, after which the temperature should not be allowed to exceed 10° until the reaction is complete. The addition requires three to four hours, provided efficient cooling is used. The citric acid should be in solution at the end of this time; if not, the stirring should be continued until it has dissolved completely.

The temperature of the reaction mixture is allowed to rise gradually until a vigorous evolution of gas commences; at this point the flask is cooled with ice water to stop the excessive frothing, but cooling is not carried far enough to stop the evolution of gas entirely (Note 3). After the more vigorous foaming has ceased, the reaction mixture is raised to about 30° and kept there until no more foaming occurs. A convenient way of determining this point is to stop the stirring for a moment and allow

the mixture to remain quiet. After a minute or so, a clear brown liquid giving off very few gas bubbles should result. This general procedure requires two to three hours.

The reaction mixture is cooled down again with ice and salt until the temperature reaches 0°, then 2400 g. of finely cracked ice is added in small portions at such a rate that the temperature does not rise above 10° until one-third of the ice has been added. Then the temperature may be allowed to rise to 25–30°. The addition of the ice requires about two hours; after this, the mixture is cooled again to 0° (Note 4) and then filtered as rapidly as possible through a funnel fitted with a filtros plate (Note 5). The crystals are thoroughly pressed and sucked as dry as possible. The acetone dicarboxylic acid is light gray to white in color. After the suction and pressing have removed practically all of the sulfuric acid, the crystals are transferred to a beaker and stirred with enough ethyl acetate (about 200 to 250 cc.) to make a thick paste. The crystals are filtered with suction. If acetone dicarboxylic acid entirely free from sulfuric acid is desired, the washing with ethyl acetate should be repeated. The yield of practically dry acetone dicarboxylic acid varies from 450–475 g. (92–97 per cent of the theoretical amount) (Note 6). This may be used directly for the preparation of the ester (p. 53). The acid itself is not stable and after a few hours gradually decomposes.

## 2. Notes

1. The reaction must be carried out in a good hood, since a large amount of carbon monoxide is liberated.

2. The use of a very efficient ice and salt mixture around the reaction flask is necessary if the reaction is to be carried out within the time indicated. It is very necessary to regulate the temperature as directed, since a considerably lower yield is obtained if the temperature rises.

3. Some cooling is necessary, or the rapid evolution of gas will cause the reaction mixture to foam over with consequent loss of material.

4. Vigorous cooling before final filtration of the acetone

dicarboxylic acid is essential to good yields, since the acid is fairly soluble in the reaction mixture.

5. The filtros plate for filtration can be very conveniently sealed into the Büchner funnel with a paste of water-glass and amorphous silica which is then hardened with concentrated sulfuric acid.

6. If the acid is to be esterified at once, careful drying from ethyl acetate is not necessary.

## 3. Other Methods of Preparation

Acetone dicarboxylic acid was first obtained by the action of concentrated sulfuric acid upon citric acid.[1] It has been made also by the gradual decomposition of a mixture of lime and sucrose.[2] The most satisfactory method, however, for producing this substance, is by the action of fuming sulfuric acid upon citric acid. Details of this preparation have been modified a number of times with the intention of improving the yield.[3]

The directions given in the above preparation are a slight modification of those given by Willstätter and Pfannenstiel.[4] While they are more complex than the details given by Ingold and Nickolls,[5] they give somewhat higher yields. The method of Ingold and Nickolls has been checked and has been found to have the advantage of requiring much less time.

[1] Ber. **17**, 2543 (1884).

[2] Ber. **26**, 3058 (1893).

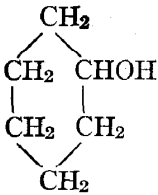
[3] Ann. **261**, 155 (1891); Gazz. chim. ital. **21**, I, 295 (1891); J. Chem. Soc. **75**, 809 Footnote (1889); **121**, 1642 (1922); Ann. **422**, 5 (1921).

[4] Ann. **422**, 5 (1921).

[5] J. Chem. Soc. **121**, 1642 (1922).

# IV

## ADIPIC ACID

 $+4\ O(HNO_3) \rightarrow CO_2H(CH_2)_4CO_2H + H_2O$

Submitted by J. F. THORPE and G. A. R. KON.
Checked by ROGER ADAMS, W. F. TULEY and C. R. NOLLER.

### 1. Procedure

A 3-l. three-necked round-bottom flask is fitted with a mechanical stirrer (Note 1), a dropping funnel, and a 90-cm. reflux water condenser carrying a tube to lead the oxides of nitrogen to a water trap or good hood. The stoppers should be made by cutting thin asbestos paper into strips about 2.5 cm. wide, moistening these in water-glass solution and then winding the strips around the end of the condenser until a stopper of the correct size is obtained. The apparatus is assembled and the stoppers are coated over with water-glass and allowed to harden over night (Note 2).

Twenty-seven hundred grams (29.9 moles) of concentrated nitric acid (sp. gr. 1.42) is placed in the flask and heated to boiling (Note 3). To the boiling solution, 500 g. (5 moles) of cyclohexanol (Note 4) is added through the separatory funnel at such a rate that it is all added in about five hours. The reaction is very vigorous at the beginning, and the cyclohexanol must be added at a rate of not more than 30 drops per minute. Toward the end, it may be added more rapidly. A large amount of oxides of nitrogen is given off during the oxidation. The reaction mix-

ture should be kept at the boiling point during the addition of the cyclohexanol and for ten to fifteen minutes longer in order to complete the reaction.

The reaction mixture is poured into a beaker and on cooling the adipic acid crystallizes. It is filtered with suction (Note 5), and the precipitate is washed once with about 200 cc. of cold water and dried in the air. The yield of slightly yellow adipic acid is 375–386 g. (55–56 per cent of the theoretical amount). This product is pure enough for most purposes. However, to remove the yellow color and obtain a purer product, this crude acid may be recrystallized from 700 cc. of concentrated nitric acid (sp. gr. 1.42). The loss in this purification is less than 10 per cent. The recrystallized acid melts at 153° (Notes 6 and 7).

## 2. Notes

1. If a mechanical stirring device is not available, the reaction may be carried out without stirring. A 5-l. flask should be used, and the mixture must be vigorously boiled to prevent the formation of a layer of cyclohexanol, which might lead to a violent reaction.

2. Corks may be used in assembling the apparatus, but they are badly attacked by the hot nitric acid and must be renewed with each run. The asbestos stoppers can be used repeatedly.

3. The nitric acid must be boiling hot, so that oxidation will set in as soon as the first drop of cyclohexanol is added. If any considerable amount of cyclohexanol is added before the oxidation starts, a serious explosion may result.

4. The cyclohexanol used was the commercial grade, which contains practically no phenol and of which 95 per cent boils between 158–163°.

5. The nitric acid mother liquors contain considerable amounts of adipic acid mixed with some glutaric acid and succinic acid. It is not practical to attempt to separate these acids by crystallization. However, by evaporating all of the nitric acid and then esterifying the resulting acid mixture with ethyl alcohol, a mixture of ethyl succinate (b. p. 121–126°/20 mm.),

ethyl glutarate (b. p. 133–138°/20 mm.), and ethyl adipate (b. p. 142–147°/20 mm.) can be obtained, from which considerable quantities of pure esters can be fractionated.

6. The nitric acid mother liquors from the purification of the first run may be used to recrystallize two or three subsequent batches of crude adipic acid, after which it may be employed as part of the acid for an oxidation.

7. Adipic acid may also be recrystallized from 2.5 times its weight of water or 50 per cent alcohol. However, the former solvent does not remove the yellow color and there is considerable loss in the mother liquors when the latter solvent is used.

## 3. Other Methods of Preparation

Adipic acid has been prepared by the following methods: the action of silver[1] or copper[2] on β-iodopropionic acid; the reduction of mucic acid with phosphorus and iodine;[3] the electrolysis of the potassium or sodium salts of monoethyl succinate;[4] the condensation of ethylene chloride or bromide with malonic ester or cyanoacetic ester and subsequent hydrolysis;[5] the oxidation of certain fractions of Baku petroleum;[6] the oxidation of cyclohexanol or cyclohexanone with nitric acid[7] or potassium permanganate.[8]

The method of Bouveault and Locquin,[9] which consists of oxidizing cyclohexanol with concentrated nitric acid, has been found to be the most useful for laboratory preparation.

[1] Ann. **149**, 221 (1869).

[2] J. Chem. Soc. **67**, 159 (1895).

[3] Ann. **125**, 20 (1863).

[4] Ann. **261**, 117 (1891); **347**, 40 (1906); Bull. soc. chim. (3) **29**, 1041 (1903).

[5] J. Chem. Soc. **65**, 578 (1894); **71**, 1063 (1897); **75**, 929 (1899); **95**, 699 (1909).

[6] Ann. **302**, 34 (1898); Ber. **32**, 1771 (1899).

[7] Rec. trav. chim. **24**, 23 (1905); Bull. soc. chim. (3) **34**, 208 (1905); (4) **3**, 438 (1908); Compt. rend. **168**, 1326 (1919).

[8] Ber. **39**, 2202 (1906); **41**, 575 (1908); **55B**, 3529 (1922); Bull. soc. chim. (4) **5**, 682 (1909).

[9] Bull. soc. chim. (4) **3**, 438 (1908).

# V

## BENZALANILINE

$$C_6H_5CHO + C_6H_5NH_2 \rightarrow C_6H_5CH{=}NC_6H_5 + H_2O$$

Submitted by Marston T. Bogert.
Checked by Henry Gilman and W. B. King.

### 1. Procedure

In a 500-cc. round-bottom flask are placed 93 g. (1 mole) of aniline and 106 g. (1 mole) of benzaldehyde (Note 1). The reaction mixture becomes quite warm and water distils. The flask is then heated in an oil bath so that the temperature of the contents is maintained at approximately 125° (Note 2) for about five hours, or until no more steam is evolved. The contents of the flask darken somewhat during the heating, but the material is homogeneous. Without cooling, the reaction mixture is slowly poured into iced water which is stirred constantly. The benzalaniline solidifies, and is filtered, washed twice with iced water, and sucked dry on the funnel. The crude wet material weighs 184–193 g. and melts at 48–50°.

The crude product, which contains considerable moisture, is purified by dissolving in boiling 95 per cent alcohol in a flask under a reflux condenser. Alcohol is added, a little at a time, until solution of the benzalaniline is complete; about 400 cc. is required. Water is then introduced into the boiling alcohol, a little at a time, until a permanent turbidity is obtained; about 150 cc. is required. The turbidity is removed by adding a few cubic centimeters of alcohol. The solution is then cooled rapidly with shaking or stirring, and the benzalaniline crystallizes (Note 3). It is filtered and then dried in the air. The yield is 154–157 g. (85–86 per cent of the theoretical amount) of a pro-

duct melting at 50–51°. By concentrating the filtrate to about 200 cc., an additional 15 g. melting at 47–50°, is obtained.

## 2. Notes

1. Both the aniline and the benzaldehyde should be freshly distilled in order to obtain the yields given in the procedure. In the distillation of the benzaldehyde, care must be taken or considerable oxidation will occur. Benzaldehyde distilled in the air contains about 0.5 per cent of benzoic acid.

2. The temperature of the reaction mixture does not exceed 110° until most of the water has been driven off.

3. Agitation is desirable during cooling, in order to prevent a brownish oil from settling to the bottom. This oil on solidification gives a dark-colored product. It is preferable to cool with iced-water.

## 3. Other Methods of Preparation

The only satisfactory method of preparing benzalaniline is the action of aniline on benzaldehyde.[1] The use of potassium pyrosulfate as a dehydrating agent, as suggested by Odell and Hines,[2] does not seem necessary.

[1] Jahresb. **1850**, 488.

[2] J. Am. Chem. Soc. **35**, 82 (1913).

## VI

## BENZALPINACOLONE

$$(CH_3)_3CCOCH_3 + C_6H_5CHO \rightarrow (CH_3)_3CCOCH = CHC_6H_5 + H_2O$$

Submitted by G. A. Hill and G. M. Bramann.
Checked by C. S. Marvel and A. B. Adams.

### 1. Procedure

In a 1500-cc. bottle are placed 100 g. (1 mole) of pinacolone (p. 91), 120 g. (1.13 moles) of freshly distilled benzaldehyde, 380 cc. of 95 per cent alcohol, 130 cc. of water, and 100 cc. of 10 per cent sodium hydroxide solution. The bottle is stoppered tightly, placed on a shaking machine, and agitated vigorously for about thirty-two hours (Note 1).

The reaction mixture is poured into a separatory funnel and diluted with an equal volume of water. The benzalpinacolone is separated by extracting three times with 300-cc. portions of benzene. The benzene extracts are combined and washed, first with water until the alkali is entirely removed, then with a saturated solution of sodium bisulfite, and finally two or three times with water. After drying over calcium chloride, the benzene is removed by distilling from a steam bath, and the residue is distilled under reduced pressure. The yield of distilled benzalpinacolone, boiling at 143–146°/10 mm. is 165–175 g. (88–93 per cent of the theoretical amount). This product is slightly yellow and melts at 41–42°. It is pure enough for most purposes. It may be recrystallized from 95 per cent alcohol and is then obtained in almost pure white crystals, melting at 43°.

### 2. Notes

1. The time may be shortened to twenty-four hours without greatly reducing the yield.

### 3. Other Methods of Preparation

Benzalpinacolone has been prepared only by the action of benzaldehyde on pinacolone in the presence of aqueous alcoholic alkalies. The method described above is a modification [1] of the original method devised by Vorländer and Kalkow.[2]

[1] J. Am. Chem. Soc. **45**, 1559 (1923).
[2] Ber. **30**, 2269 (1897).

## VII

# $p$-BROMOACETOPHENONE

$$C_6H_5Br + (CH_3CO)_2O + (AlCl_3) \rightarrow (p)\,BrC_6H_4COCH_3 + CH_3CO_2H$$

Submitted by ROGER ADAMS and C. R. NOLLER.
Checked by J. B. CONANT and C. R. KINNEY.

## 1. Procedure

IN a 5-l. round-bottom three-necked flask, fitted with a mechanical stirrer, separatory funnel, and reflux condenser holding a tube to carry off the evolved hydrogen chloride, is placed 392 g. (2.5 moles) of bromobenzene in 1-l. of dry carbon disulfide (Note 1). To this is added 750 g. (5.6 moles) (Note 2) of anhydrous aluminium chloride. The mixture is heated on a steam bath until gentle refluxing starts, and then 204 g. (2 moles) of acetic anhydride (Note 3) is added slowly through the dropping funnel. The time of addition is about one hour. Gentle refluxing should be continued throughout the time of addition of the anhydride and for an hour afterward. The reaction is accompanied by a copious evolution of hydrogen chloride which does not entirely cease even after this subsequent heating.

A condenser is attached to one of the side necks, and the carbon disulfide is distilled without removing the flask from the steam bath. After the removal of the solvent (Note 4), the reaction mixture is allowed to cool somewhat (Note 5); but while it is still warm, it is poured slowly with stirring over cracked ice to which hydrochloric acid has been added. In this way only a small amount of the aluminium chloride addition product remains in the flask. This is decomposed with ice and hydrochloric acid and added to the main product. The volume is now about 5 l. Each 2-l. portion is extracted twice with 300-cc.

and 200-cc. portions of benzene or ether. The extracts are combined and washed twice with water, once with 10 per cent sodium hydroxide solution, and twice more with water. The final water washings should be practically colorless and the separation sharp, allowing any precipitate to separate with the water. The extract is dried for an hour with about 30 g. of calcium chloride and filtered, and the solvent is distilled from a steam bath. Then the residue is distilled under reduced pressure with a short column (Org. Syn. **1**, 40). Some low-boiling material comes over first, and then the temperature rises rapidly. If care has been taken in the water decomposition to remove all of the aluminium salts (Note 6), the product comes over water-white and crystallizes to a white solid melting at 49–50.5°. The yield is 340–395 g. of a product boiling over a three-degree range (69–79 per cent of the theoretical amount). On redistillation the boiling point is 117°/7 mm.; 129–130°/15 mm.; and 255.5°/736 mm.

## 2. Notes

1. If the carbon disulfide-bromobenzene solution is not clear it should be dried over calcium chloride and filtered before the aluminium chloride is added. In using such large amounts of carbon disulfide, particular precautions must be taken to prevent fires.

2. The aluminium chloride should be added in about this excess. When the excess is larger the yield does not seem to be increased, and when only 2 equivalents are used it is diminished by 10 to 15 per cent.

3. The acetic anhydride should boil at 136–139°. Some commercial grades are satisfactory, whereas others have been found to contain almost 50 per cent of acetic acid.

4. About 600 to 800 cc. of carbon disulfide is recovered and may be used in the next run.

5. If the product is allowed to come to room temperature before decomposition with water, it becomes semi-solid and is not easily removed from the flask.

6. If the aluminium chloride double compound is not entirely

decomposed by water and the aluminium salts thus removed, the distillate comes over slightly red and does not crystallize well on cooling. Redistillation, however, gives a pure product.

7. This method is an improvement over the older methods for the preparation of substituted acetophenone derivatives. The yields obtained by the use of acetyl chloride in place of acetic anhydride in the preparation of *p*-bromoacetophenone were invariably lower.

8. Under the same general conditions, satisfactory yields of other acetophenones may be obtained. Thus, from 281 g. of chlorobenzene, 750 g. of aluminium chloride, and 205 g. of acetic anhydride, a consistent yield of 285 to 300 g. (70–73 per cent of the theoretical amount) of *p*-chloroacetophenone, boiling at 124–126°/24 mm. and melting at 20–21°, is obtained. Similarly, acetophenone may be obtained in 76–83 per cent yields, *p*-methylacetophenone in 85–89 per cent yields, and *p*-methoxyacetophenone in 90–94 per cent yields.

## 3. Other Methods of Preparation

*p*-Bromoacetophenone has been made by the action of acetyl chloride in carbon disulfide on bromobenzene in the presence of anhydrous aluminium chloride,[1] and by the use of acetic anhydride in place of the acetyl chloride.[2]

[1] Ber. **24**, 550, 3766 (1891); J. Am. Chem. Soc. **35**, 266 (1913).
[2] J. Am. Chem. Soc. **46**, 1892 (1924).

## *p*-BROMOTOLUENE

$$(p)\ CH_3C_6H_4NH_2 + HNO_2 + H_2SO_4 \rightarrow (p)\ CH_3C_6H_4N_2SO_4H + 2H_2O$$

$$(p)\ CH_3C_6H_4N_2SO_4H + HBr + (CuBr) \rightarrow (p)\ CH_3C_6H_4Br + N_2 + H_2SO_4$$

Submitted by LUCIUS A. BIGELOW.
Checked by C. S. MARVEL and A. E. BRODERICK.

### 1. Procedure

A MIXTURE of 63 g. (0.25 mole) of crystallized cupric sulfate, 20 g. (0.31 mole) of copper turnings, 154 g. (1.1 moles) of sodium bromide, 30 g. (0.28 mole) of concentrated sulfuric acid (sp. gr. 1.84), and 1 l. of water is refluxed over a flame for three to four hours until the color becomes yellowish (Note 1).

When the hydrobromic acid-cuprous bromide solution is ready for use, the diazonium solution is prepared. A solution of 107 g. (1 mole) of *p*-toluidine and 196 g. (1.9 moles) of concentrated sulfuric acid (sp. gr. 1.84) in 1 l. of water is cooled below 20° and diazotized with a solution of 70 g. (1 mole) of sodium nitrite in 125 cc. of water. This requires about twenty to thirty minutes when the temperature is maintained between 15° and 20° by means of an ice bath.

A 5-l. round-bottom flask containing the hydrobromic acid-cuprous bromide solution, is arranged for steam distillation. After the copper solution is heated to boiling, the diazonium solution is gradually added from a separatory funnel and a vigorous current of steam is passed through the reaction mixture at the same time. This procedure requires about two hours.

The aqueous distillate is made alkaline with sodium hydroxide solution and the *p*-bromotoluene is separated from the water layer (Note 2). The crude product weighs 131–137 g. For purification the crude product is washed once with concentrated sulfuric acid (Note 3) and then with water. It is dried over a little calcium chloride, filtered, and distilled. The yield of pure product amounts to 120–126 g. (70–73 per cent of the theoretical amount) boiling at 183–185° and melting at 25–26°.

## 2. Notes

1. If the color of the solution has not been discharged after heating for three to four hours, a few grams of sodium sulfite may be added to complete the reduction.

2. A small amount of ether or benzene may be used to aid in the separation if it is needed.

3. The sulfuric acid treatment is necessary if a colorless product is to be obtained. If ether is used in the extraction of the *p*-bromotoluene, it must be removed before washing with sulfuric acid.

## 3. Other Methods of Preparation

*p*-Bromotoluene has been obtained by the bromination of toluene with bromine in the presence of various catalysts [1] and with hypobromous acid.[2] The best method for its preparation, however, is the diazotization of *p*-toluidine followed by replacement of the diazonium group by bromine.[3]

[1] Ann. **136**, 301 (1865); **154**, 294 (1870); **242**, 165 (1887); Z. Chem. **1869**, 138; Ber. **18**, 608 (1885); Compt. rend. **158**, 1806 (1914).

[2] Ber. **43**, 673 (1910).

[3] Ber. **37**, 994 (1904).

## n-BUTYL n-BUTYRATE

$$6C_4H_9OH + 2Na_2Cr_2O_7 + 8H_2SO_4 \rightarrow 3C_3H_7CO_2C_4H_9 + 2Cr_2(SO_4)_3 + 2Na_2SO_4 + 14H_2O$$

Submitted by G. Ross Robertson.
Checked by Henry Gilman and J. E. Kirby.

### 1. Procedure

In a 2-l. flask fitted with a mechanical stirrer, a thermometer, and a dropping funnel, are placed a cool solution of 240 cc. (4.3 moles) of commercial sulfuric acid (sp. gr. 1.84) in 240 cc. of water, and 240 g. (3.21 moles) of technical *n*-butyl alcohol (Note 1). The whole is placed in a large, efficient ice-salt bath.

A solution of 320 g. (1.07 moles) of crystalline sodium dichromate (350 g. of the ordinary moist technical hydrated salt is also suitable) in 200 cc. of water is dropped from the funnel into the vigorously stirred alcohol mixture as rapidly as can be done without running the temperature above 20°. When most of the dichromate has been added, the viscosity of the reaction mixture becomes so great that the stirring is rendered inefficient. The temperature is now allowed to rise to 35° if necessary (Note 2), to accelerate the reaction.

The resulting green syrupy emulsion is diluted with an equal volume of water, whereupon 220–225 cc. of an oil containing the desired ester (Note 3), slowly separates. This oil is washed three times with water, separated, and treated with a few grams of anhydrous sodium sulfate in order to remove most of the water. It is now distilled slowly through a large, efficient fractionating column. The fraction boiling at 150–170° is collected, and should amount to 170–175 cc. It is washed with

five 15-cc. portions of 60 per cent sulfuric acid (sp. gr. about 1.5) (Note 4), is then washed free of acids with dilute sodium hydroxide, and finally washed free of alkali with cold water. It is rapidily dried, as before, with sodium sulfate, and fractionated through the same distilling column. The fraction boiling at 162–166° (uncorr.) consists of *n*-butyl *n*-butyrate, containing a small percentage of residual butyl alcohol. The yield is 96–110 g. (41–47 per cent of the theoretical amount).

If higher purity is desired, the fractionation must be repeated. An additional yield may be secured by further fractionation of the lower-boiling fractions (Note 5).

## 2. Notes

1. When *n*-butyl alcohol is oxidized to butyric acid in the presence of a high concentration of sulfuric acid, esterification takes place at once, even in the cold, as long as an excess of the alcohol is present.

2. If the temperature of the reaction mixture is allowed to rise much above 35°, considerable material escapes in the form of butyraldehyde (b. p. 74°).

3. The oil obtained as the first crude product contains, in addition to the desired ester, much unchanged butyl alcohol, a little butyraldehyde, and a little free butyric acid.

4. The 60 per cent sulfuric acid is chosen as a wash liquid because it is miscible with butyl alcohol but not with the ester. The volatile aldehyde disappears in the two fractionations, while the butyric acid is removed by the alkali.

5. The low-boiling fractions could no doubt be returned to a new batch if this process were carried out repeatedly in quantity production. About 25 per cent of the original butyl alcohol can be recovered if desired. The very small fractions boiling above 166° may contain esters of other alcohols occurring in the technical product used, and possibly butyl succinate and related by-products.

### 3. Other Methods of Preparation

*n*-Butyl *n*-butyrate has been made by the interaction of *n*-butyl alcohol and *n*-butyric acid in the presence of sulfuric acid,[1] and by the action of *n*-butyl iodide on silver *n*-butyrate.[2]

[1] Ann. **233**, 269 (1886).
[2] Ann. **158**, 170 (1871).

# X

## n-BUTYL CHLORIDE

$$CH_3(CH_2)_2CH_2OH + HCl + (ZnCl_2) \rightarrow CH_3(CH_2)_2CH_2Cl + H_2O$$

Submitted by J. F. NORRIS.
Checked by C. S. MARVEL and W. D. LANSING.

### 1. Procedure

To 190 g. (2 moles) of cold concentrated hydrochloric acid (sp. gr. 1.19) is added 272 g. (2 moles) of anhydrous zinc chloride. The mixture is kept cold to avoid loss of hydrogen chloride. To this solution, 74 g. of n-butyl alcohol (1 mole) is added (Note 1). The mixture is then refluxed over a free flame for three and one-half to four hours (Note 2). After cooling, the upper layer is separated (Note 3) and placed in a distilling flask with an equal volume of concentrated sulfuric acid (Note 4). The side arm of the flask is closed and the neck is connected with a reflux condenser. After refluxing gently for one-half hour, the chloride is distilled. The distillate is washed with water, dried over calcium chloride, filtered, and distilled. The fraction boiling at 76–78° weighs 59–61 g. (64–66 per cent of the theoretical amount).

### 2. Notes

1. The best results were obtained when the substances were used in the molecular ratio: 1 of alcohol, 2 of hydrogen chloride as concentrated hydrochloric acid, and 2 of zinc chloride.

2. Shorter periods of heating diminish the yields. Heating on a steam bath also gives lower yields. The mixture should be boiled rather vigorously over a flame. With larger runs, an even longer heating period must be used. It is necessary to boil a

5-mole alcohol run for nine hours to obtain the yield mentioned in the procedure.

3. The zinc chloride may be recovered from the aqueous solution by evaporation until a syrupy residue is obtained. This may be used in the next run.

4. This treatment with sulfuric acid is carried out in order to remove high-boiling impurities that are not easily separated by fractional distillation.

5. Other alkyl chlorides may be prepared by this general procedure.[12] The following yields are obtained with some of the common alcohols, used in the molecular proportions given under the procedure: *n*-propyl chloride, 55–61 per cent; iso-propyl chloride, 70–76 per cent; *sec.*-butyl chloride, 60–65 per cent; 2-chloropentane, 60–70 per cent.

### 3. Other Methods of Preparation

Alkyl chlorides have been obtained by the direct chlorination of hydrocarbons [1] and by the addition of hydrogen chloride to olefines.[2] However, they have usually been prepared from the corresponding alcohol by the action of a number of reagents, such as dry hydrogen chloride,[3] dry hydrogen chloride in the presence of zinc chloride,[4] phosphorus trichloride,[5] phosphorus oxychloride,[6] phosphorus pentachloride,[7] phosphorus trichloride

[1] Ann. chim. phys. (3) **52**, 98 (1858); Jahresb. **1863**, 524; Ann. **131**, 76 (1864); **132**, 234 (1864); **144**, 186 (1867); **150**, 210 (1869); **152**, 159 (1869); **161**, 265 (1871); Am. Chem. J. **19**, 245 (1897); Ber. **31**, 1802 (1898); J. prakt. Chem. (2) **59**, 562 (1899).

[2] Ann. **127**, 71 (1863); **189**, 51 (1877); **196**, 124 (1879); Ann. chim. phys. (4) **3**, 161 (1864); U. S. Pat. 1,518,182; Chem. Zentr. **1925**, I, 1129.

[3] Ann. **52**, 312 (1844); **152**, 5 (1869); **158**, 160 (1871); **159**, 72 (1871); **189**, 3 (1877); **190**, 312 (1878); **351**, 188 (1907); Z. Chem. **1871**, 147; Bull. soc. chim. (3) **1**, 603 (1889); (3) **2**, 136 (1889); (3) **25**, 844 (1901); Monatsh. **28**, 559 (1907); U. S. Pat. 1,440,683; C. A. **17**, 1029 (1923).

[4] Ann. **174**, 372 (1874); Ber. **7**, 741 (1874); J. prakt. Chem. (2) **14**, 196 (1876); Ann. chim. phys. (6) **19**, 406 (1890); U. S. Pat. 1,509,463; Chem. Zentr. **1925** I, 573.

[5] J. Russ. Phys. Chem. Soc. **29**, 223 (1897); Chem. Zentr. **1897**, II, 334; J. Chem. Soc. **87**, 1594 (1905).

[6] Ann. **102**, 334 (1857); Ber. **6**, 35 (1873).

[7] Ann. **37**, 164 (1841); **92**, 398 (1854); **103**, 81 (1857); **163**, 266 (1872); **177**, 183 (1875); **179**, 321 (1875); **183**, 348 (1876); **190**, 336 (1878); **191**, 131 (1878).

in the presence of zinc chloride,[8] sodium chloride and sulfuric acid,[9] aqueous hydrochloric acid,[10] and aqueous hydrochloric acid in the presence of calcium chloride.[11] The method above described is more convenient than the older methods using anhydrous hydrogen chloride, and better yields are obtained than can be had by the use of aqueous hydrochloric acid with other catalysts.[12]

[8] J. Am. Chem. Soc. **29**, 1328 (1907).

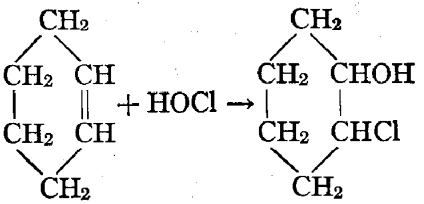
[9] Ann. **15**, 17 (1835).

[10] Am. Chem. J. **38**, 641 (1907); J. Am. Chem. Soc. **38**, 1071 (1916); **42**, 2093 (1920).

[11] Ger. Pat. 280,740; Frdl. **12**, 22 (1914).

[12] J. Am. Chem. Soc. **46**, 753 (1924).

# o-CHLOROCYCLOHEXANOL



Submitted by G. H. COLEMAN and H. F. JOHNSTONE.
Checked by C. S. MARVEL and A. B. ADAMS.

## 1. Procedure

To a solution of 25 g. of mercuric chloride in 500 cc. of water in a 5-l. flask, 800 g. of cracked ice is added. A cold solution of 190 g. of sodium hydroxide in 500 cc. of water is added, and a rapid stream of chlorine is passed into the mixture, which must be kept below 5°. The addition of chlorine is continued in this way until the yellow precipitate of mercuric oxide just disappears. Then 600 cc. of cold nitric acid (1.5 N) is added slowly, with stirring.

The concentration of the hypochlorous acid solution is determined by adding a measured volume to an excess of potassium iodide solution acidified with hydrochloric acid, and titrating with standard thiosulfate solution. Usually the concentration is found to be between 3.5 and 4 per cent. The amount necessary to react with 123 g. (1.5 moles) of cyclohexene is calculated.

In a 5-l. round-bottom flask equipped with a good mechanical stirrer (Note 1), is placed 123 g. (1.5 moles) of cyclohexene (p. 33), and to it is added about one-fourth the calculated amount of the hypochlorous acid solution. The mixture is kept below 15° and stirred vigorously until a 1-cc. test portion gives no yellow

color when it is treated with potassium iodide solution and dilute hydrochloric acid. When the first portion of the hypochlorous acid has reacted, a second is added and the process is repeated. When all the hypochlorous acid has been added and the reaction is complete, the oily layer should be on the bottom and a very slight excess of hypochlorous acid should be present, as indicated by the potassium iodide test. If these conditions are not fulfilled, 100-cc. portions of the hypochlorous acid solution are added until the reaction is shown to be complete.

The solution is now saturated with salt and distilled with steam (Note 2). About 2 l. of distillate is required before all of the *o*-chlorocyclohexanol passes over. The distillate is saturated with salt and the oily layer separated. The aqueous layer is extracted once with about 250 cc. of ether. This is added to the main portion, which is dried with anhydrous sodium sulfate. The ether is removed by distillation and the product distilled under reduced pressure. The fraction boiling between 88–90°/20 mm. (104–106°/45 mm.) is collected. The yield is 142–148 g. (70–73 per cent of the theoretical amount).

## 2. Notes

1. If a mechanical stirrer is not available, shaking the flask by hand will give as good results.

2. In the separation of the product from the hypochlorous acid solution, steam distillation seems to be desirable. In several runs in which this was not carried out, a larger amount of a dark-colored high-boiling residue remained in the flask after distillation, and the yield of *o*-chlorocyclohexanol was smaller.

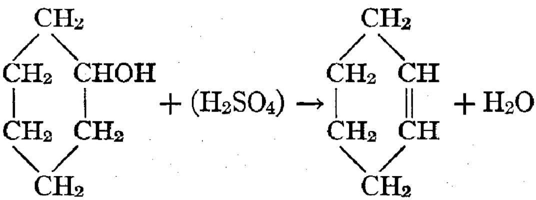
## 3. Other Methods of Preparation

*o*-Chlorocyclohexanol has been prepared only by the action of hypochlorous acid on cyclohexene.[1] The methods that have been given in the literature differ mainly in the manner in which the hypochlorous acid is obtained. The yields are practically the same by all of the procedures.

[1] J. Chem. Soc. **73**, 948 (1898); J. Am. Chem. Soc. **42**, 2621 (1920); Bull. soc. chim. (4) **31**, 177 (1922).

XII

# CYCLOHEXENE



Submitted by G. H. Coleman and H. F. Johnstone.
Checked by C. S. Marvel and A. B. Adams.

## 1. Procedure

In a 500-cc. modified Claisen flask (Org. Syn. 1, 40) are placed 400 g. of cyclohexanol (Note 1) and 12 cc. of concentrated sulfuric acid, and the flask is connected to a condenser and receiver. It is then placed in an oil bath which is heated to a temperature of 130–140°. The distillation is continued until only a small residue remains and the odor of sulfur dioxide is apparent. Toward the end of the distillation the temperature of the bath may be raised to 150°. The receiver is surrounded with an ice bath (Note 2) during the entire distillation which requires from five to six hours.

The distillate is saturated with salt, and the cyclohexene is separated from the water layer. It is dried with calcium chloride and fractionated through an efficient column. The fraction boiling at 80–82° (uncorr.) is collected separately. It may be necessary to refractionate the low- and high-boiling portions once or twice. The high-boiling fraction is finally added to the next run. The yield of cyclohexene is 260–285 g. (78–87 per cent of the theoretical amount.)

## 2. Notes

1. The ordinary commercial grade of cyclohexanol was used in these experiments. It contained no more than a trace of phenol and 90–95 per cent of it distilled at 158–163°.

2. In transferring cyclohexene, it is best to keep it well cooled to avoid small losses by evaporation.

## 3. Other Methods of Preparation

The practical method of preparing cyclohexene is the dehydration of cyclohexanol. Many reagents have been used for this purpose. The following is a partial list: potassium bisulfate,[1] oxalic acid,[2] sulfuric acid,[3] *p*-toluene sulfonic acid,[4] and iodine.[5] In addition, cyclohexanol has been dehydrated at high temperatures over various catalysts.[6]

The method described in the procedure is a slight modification of one that was first devised by Senderens [7] and later modified by Kendall and Osterberg.[8]

[1] Bull. soc. chim. (3) **33**, 270 (1905); Ber. **45**, 1466 (1912).

[2] Ber. **34**, 3252 (1901); **45**, 1466 (1912); J. Russ. Phys. Chem. Soc. **43**, 1222 (1911); Chem. Zentr. **1912**, I, 139; Bull. soc. chim. (4) **17**, 174 (1915).

[3] Compt. rend. **154**, 1169 (1912); J. Am. Chem. Soc. **42**, 2620 (1920).

[4] Bull. soc. chim. Belg. **26**, 304 (1912); Chem. Zentr. **1912**, II, 1006.

[5] J. Am. Chem. Soc. **37**, 1754 (1915).

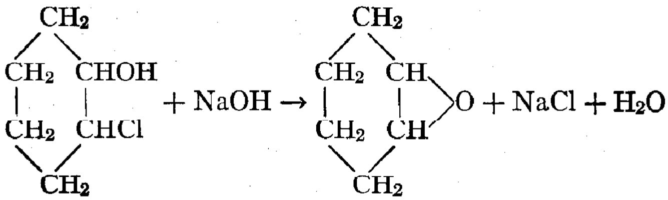
[6] Ber. **43**, 3385 (1910); Ger. Pat. 241,895; Frdl. **10**, 1032 (1911); Ann. chim. phys. (8) **25**, 461, 500 (1912).

[7] Compt. rend. **154**, 1169 (1912).

[8] J. Am. Chem. Soc. **42**, 2620 (1920).

# XIII

## CYCLOHEXENE OXIDE



Submitted by A. E. OSTERBERG.
Checked by C. S. MARVEL and A. B. ADAMS.

### 1. Procedure

IN a 2-l. round-bottom flask fitted with a mechanical stirrer, is placed a solution of 70 g. (1.75 moles) of sodium hydroxide in 400 cc. of water. To this solution is then added 230 g. (1.71 moles) of *o*-chlorocyclohexanol (p. 31). The mixture is stirred vigorously for about one hour (Note 1). The stirring is then stopped and the upper layer is separated and fractionated carefully through an efficient column.

The fractions collected are 100–129°, 129–134°, and 134–175° (Note 2). The first fraction is mainly cyclohexene oxide but contains some water which is separated with a separatory funnel before the second fractionation. After the fraction boiling at 100–129° is collected, the condenser should be removed and dried thoroughly before collecting the second fraction, in order to insure anhydrous material. After two or three fractionations, the yield of cyclohexene oxide boiling at 129–134° is 117–122 g. (70–73 per cent of the theoretical amount).

## 2. Notes

1. If the stirring is continued for much longer than one and one-half hours, the yield may be lessened somewhat.

2. There is a slight high-boiling residue which begins to decompose if the temperature is raised above this point. The products of decomposition are hard to remove from the distilling flask.

## 3. Other Methods of Preparation

Cyclohexene oxide was first prepared by Brunel from *o*-iodocyclohexanol and solid potassium hydroxide.[1] It has also been obtained by the oxidation of cyclohexene with benzoyl hydroperoxide.[2]

[1] Compt. rend. **136**, 384 (1903); **137**, 62 (1903); Bull. soc. chim. (3) **29**, 883 (1903).

[2] Compt. rend. **174**, 462 (1922).

# XIV

## CYCLOPENTANONE

$$CO_2H(CH_2)_4CO_2H \rightarrow \begin{array}{l} CH_2-CH_2 \\ | \qquad\quad \rangle CO + H_2O + CO_2 \\ CH_2-CH_2 \end{array}$$

Submitted by J. F. Thorpe and G. A. R. Kon.
Checked by Roger Adams and C. R. Noller.

### 1. Procedure

In a 1-l. distilling flask (Note 1) fitted with a thermometer reaching within 5 mm. of the bottom, is placed an intimate mixture of 200 g. of powdered adipic acid (Note 2) and 10 g. of finely ground crystallized barium hydroxide. The mixture is gradually heated in a fusible alloy bath (Note 3) to 285–295° (Note 4) during about one and one-half hours, and maintained at that temperature until only a small amount of dry residue remains in the flask. This requires about two hours longer. The cyclopentanone distils slowly, accompanied by small quantities of adipic acid.

The ketone is separated from the water in the distillate, either by salting out with calcium chloride or by extraction with a little ether. It is washed with a little aqueous alkali and then with water, dried over calcium chloride, and distilled through a good fractionating column (Note 5). The fraction boiling at 128–131° is cyclopentanone. The yield is 86–92 g. (75–80 per cent of the theoretical amount).

### 2. Notes

1. If larger runs are made, a three-neck flask provided with a mechanical stirrer should be used for the reaction.

2. The unrecrystallized adipic acid, prepared as described on page 9, may be used.

3. An air bath may be used, but the metal bath insures better temperature control.

4. If the temperature goes above 300°, the adipic acid begins to distil quite rapidly. It is best to hold the temperature as near 290° as is possible.

5. Cyclopentanone is quite volatile with ether vapor, and careful fractionation is necessary when ether is used for the separation of the ketone from the water.

### 3. Other Methods of Preparation

Cyclopentanone has been prepared from adipic acid by distilling the calcium salt,[1] heating alone [2] or with acetic anhydride,[3] or in the presence of various catalysts such as barium hydroxide,[4] thorium oxide,[5] manganous oxide,[5] uranium nitrate,[6] ferrous sulfate [6] and others.[7]

[1] Ann. **275**, 312 (1893); Rec. trav. chim. **24**, 23 (1905).
[2] Ber. **45**, 1605 (1912).
[3] Compt. rend. **144**, 1357 (1907); Ann. chim. phys. (8) **26**, 43 (1912).
[4] Ger. Pat. 256,622; Frdl. **11**, 49 (1913); Ann. **410**, 36 (1915).
[5] Compt. rend. **158**, 987 (1914).
[6] Ger. Pat. 256,622; Frdl. **11**, 49 (1913).
[7] Compt. rend. **168**, 1326 (1919).

XV

## *l*-CYSTINE

Hydrolysis of Keratin from Hair$\longrightarrow$

$$CO_2HCH(NH_2)CH_2SSCH_2CH(NH_2)CO_2H$$

Submitted by R. A. Gortner and W. F. Hoffman.
Checked by H. T. Clarke and E. E. Dreger.

### 1. Procedure

Human hair (Note 1) is freed from foreign matter (Note 2), washed well with a lukewarm solution of soap (Note 3), then twice with cold distilled water, and dried. This washing removes the natural oils from the hair (Note 4). Two kilos of the dry, washed hair is pushed into a 12-l. round-bottom Pyrex flask, and 4 l. of 20 per cent hydrochloric acid (Note 5) is added. An air-cooled reflux condenser, consisting of a wide glass tube, is attached to the flask. The hair is hydrolyzed by heating on the steam bath (Note 6) until the biuret reaction is entirely negative; this requires one hundred twenty to one hundred forty-four hours.

The mixture is filtered hot and the insoluble residue is washed with distilled water. The total filtrate is now partially neutralized with 300 cc. of 40 per cent sodium hydroxide solution, while the mixture is well stirred and cooled, and then a saturated solution of 3750 g. of crystallized sodium acetate is added. The Congo Red test for mineral acid should then be entirely negative. Care must be taken *not to make the solution alkaline* with sodium hydroxide (Note 7). After standing for three days at room temperature, the precipitated cystine is filtered on a suction funnel. This crude material, containing in addition to the

cystine, some "humin," pigments, and tyrosine, is dissolved in 3 l. of 3 per cent hydrochloric acid. The solution is filtered and competely decolorized by two to five treatments with 20–25 g. portions of decolorizing carbon (Norit) which has been completely freed from calcium phosphate by boiling with dilute hydrochloric acid and washing with cold water. The filtrate after decolorizing should be water-clear, or at the most only slightly yellow. If it shows more color, the treatment with decolorizing carbon should be carried out again. The solution should finally be filtered once by gravity to remove traces of a solid impurity which is apt to pass through the suction funnel. The cystine is precipitated from the clear solution by adding a filtered saturated solution of 900–1000 g. of crystallized sodium acetate until the Congo Red reaction is negative. After standing five to six hours (Note 8), the cystine is filtered and washed twice with 100–200 cc. portions of hot, distilled water to remove the last traces of tyrosine. By this method the typical colorless hexagonal plates of cystine are obtained. The yield is 100–106 g. (5.0–5.3 per cent of the weight of the starting material).

## 2. Notes

1. Crude sheep's wool may also be employed, but the yield is not so high (about 2.6 per cent).

2. Hair obtained from barber shops generally contains matches, paper, cigar and cigarette butts, and similar impurities which should be sorted out by hand as completely as possible. The other principal contamination is sand which causes little trouble and need not be removed.

3. A high grade of soap should be employed. Hair kept in hot dilute sodium carbonate solution for one to two hours yields little or no cystine.

4. The oily material may also be removed by extracting with gasoline or benzene, but this procedure involves considerably more labor.

5. The constant-boiling (20 per cent) hydrochloric acid may be prepared by adding 2000 cc. of water to 2700 cc. of concentrated hydrochloric acid (sp. gr. 1.20).

6. The hydrolysis can be carried out in a much shorter time by heating over a flame or on a sand bath, but there is great danger of breaking the flask on account of bumping.

7. An alkaline reaction must always be avoided, as even dilute sodium carbonate decomposes cystine.

8. If the mixture is allowed to stand for a longer time, tyrosine tends to crystallize out with the cystine.

### 3. Other Methods of Preparation

*l*-Cystine has been obtained by the hydrolysis of a large number of proteins. However, the keratins are the only common proteins rich enough in cystine to serve as a source for this amino acid. Many investigators have devised methods for its isolation from the hydrolytic products of human hair,[1] wool,[2] horn,[3] nail,[3] feathers,[3] and horse hair.[4] The method of Folin [5] is the basis for most of the others. The present method does not claim to give as high a yield as some of those reported in the literature, but is convenient and gives consistent results.

[1] Z. physiol. Chem. **34**, 225 (1902); **52**, 475 (1907); Beitr. Chem. Physiol. Path. **3**, 16 (1903); J. Biol. Chem. **9**, 369 (1911); **55**, 671 (1923); J. prakt. Chem. (2) **95**, 360 (1917); J. Am. Chem. Soc. **44**, 346 (1922); C. A. **17**, 293 (1923).

[2] Z. physiol. Chem. **52**, 360 (1907); J. Biol Chem. **8**, 10 (1910); J. Am. Chem. Soc. **43**, 2692 (1921); **44**, 346 (1922); C. A. **17**, 293 (1923).

[3] Z. physiol. Chem. **28**, 599 (1899); **32**, 97 (1901); **34**, 218 (1902); **52**, 367, 479 (1907); **69**, 310 (1910); Beitr. Chem. Physiol. Path. **3**, 15 (1903); J. Biol. Chem. **9**, 369 (1911).

[4] Z. physiol. Chem. **39**, 352 (1903); Fischer, Anleitung zur Darstellung org. Präp. 9th Ed. page 93.

[5] J. Biol. Chem. **8**, 10 (1910).

# XVI

## DIALLYL AMINE

$$(CH_2{=}CHCH_2)_2NCN + 2H_2O \rightarrow (CH_2{=}CHCH_2)_2NH + NH_3 + CO_2$$

Submitted by E. B. VLIET.
Checked by ROGER ADAMS and E. E. DREGER.

### 1. Procedure

A SOLUTION of 123 g. (1.2 moles) of sulfuric acid (sp. gr. 1.84) in 370 cc. of water is placed in a 2-l. round-bottom flask equipped with a reflux condenser. To this is added 98.5 g. (0.8 mole) of diallyl cyanamide (p. 45) and a few pieces of clay plate to prevent bumping. The mixture is refluxed gently for six hours. During the first fifteen minutes of heating, some bumping occurs. However, the mixture gradually becomes homogeneous and the boiling then proceeds smoothly (Note 1).

After six hours, the solution is cooled to room temperature and a cold solution of 192 g. (4.8 moles) of sodium hydroxide in 350 cc. of water is poured down the side of the flask so that most of it settles to the bottom without mixing with the solution in the flask. The flask is then connected to a condenser for downward distillation and is shaken to mix the two layers. The resulting free amine separates. The flask is heated and the amine, together with some water, distils. The distillation is continued until no amine separates from a test portion of the distillate. There is a small quantity of an oily liquid left floating in the flask. This is probably an impurity from the diallyl cyanamide.

The weight of water in the distillate is estimated, and about one-half of this amount of potassium hydroxide is added in the form of sticks, so that it will dissolve slowly. The mixture should

be kept cool while the potassium hydroxide is dissolving. Bubbles of ammonia gas will be evolved. When solution of the potassium hydroxide is complete, the amine is separated and dried for several hours over solid sodium hydroxide which has been freshly broken up into small lumps. It is then filtered into a distilling flask and distilled at atmospheric pressure. If the product has been thoroughly dried, there should be no low-boiling material. All of the diallyl amine should come over at 108–111° and only a very small amount of higher-boiling material should remain. The yield is 62–68 g. (80–86 per cent of the theoretical amount).

## 2. Notes

1. Alkali may be used for this hydrolysis instead of acid; but it is not as satisfactory, since the reaction mixture remains in two layers, thus causing the hydrolysis to proceed more slowly. Furthermore, any slight leak in the apparatus during refluxing permits a loss of product.

2. This reaction represents a general method for the preparation of secondary amines; thus, di-*n*-butyl amine has been obtained from di-*n*-butyl cyanamide in yields of 75 per cent of the theoretical amount.

## 3. Other Methods of Preparation

Diallyl amine has been prepared from allyl amine and allyl bromide,[1] and from allyl amine and allyl chloride.[2] Experiments on these methods showed that the resulting product contained relatively large amounts of triallyl amine and monoallyl amine and it was very difficult to isolate pure diallyl amine. The above synthesis from diallyl cyanamide, which has recently appeared in the literature,[3] is more satisfactory than the older methods.

[1] Ber. **14**, 1879 (1881).

[2] Ber. **16**, 1641 (1883).

[3] J. Am. Chem. Soc. **46**, 1307 (1924); Versuche mit Diallylderivaten, Dissertation von Paul Graf, Eidgenossischen Technischen Hochschule, Zurich; page 29.

XVII

## DIALLYL CYANAMIDE

$$CaNCN + 2NaOH \rightarrow Ca(OH)_2 + Na_2NCN$$

$$Na_2NCN + 2CH_2{=}CHCH_2Br \rightarrow (CH_2{=}CHCH_2)_2NCN + 2NaBr$$

Submitted by E. B. VLIET.
Checked by ROGER ADAMS and E. E. DREGER.

### 1. Procedure

IN a 5-l. round-bottom two-necked flask, fitted with a reflux condenser and a mechanical stirrer with a mercury seal, are placed 660 cc. of cold water and 135 g. of cracked ice. Two hundred grams (containing about 1.4 moles of pure calcium cyanamide) of fresh lime nitrogen (Note 1) is added slowly, with stirring. As soon as the lime nitrogen is suspended thoroughly in the water, a cold solution of 110 g. (2.75 moles) of sodium hydroxide in 200 cc. of water is added slowly, with stirring. Then the suspension is stirred quite briskly during one hour. If the temperature rises above 25°, small amounts of ice should be added (Note 2).

To the solution of sodium cyanamide thus prepared, 380 g. (3.14 moles) of allyl bromide (Note 3) and 660 cc. of 95 per cent alcohol are added. The mixture is then heated on a water bath with good stirring until it refluxes gently, and the heating and stirring are continued for two and one-half hours. Then the reflux condenser is replaced by one set downward for distillation. The stirring is continued and the alcohol is distilled until about 500 cc. has been collected. The distillate may be discarded or used for the recovery of alcohol (Note 4).

The reaction mixture is cooled to room temperature and filtered with suction through a large Büchner funnel. The residue

is washed with alcohol. The filtrate which will be in two layers, is extracted twice with benzene first with 270 cc. and then with 130 cc. The combined benzene extracts are dried with sodium sulphate and then filtered into a distilling flask. The benzene is distilled from a water bath, and then the diallyl cyanamide is distilled under reduced pressure. It boils at 105–110°/18 mm.; at 128–133°/57 mm.; and at 140–145°/90° mm. There is a small residue of higher-boiling material. The yield of diallyl cyanamide, boiling over a five-degree range, is 90–97 g. (52–56 per cent of the theoretical amount based on the calcium cyanamide).

## 2. Notes

1. The lime nitrogen used in this preparation should be the crude, untreated, product sold as fertilizer under the name "Cyanamid." It contains approximately 55 per cent calcium cyanamide, 20 per cent calcium oxide, 12 per cent graphite, and small amounts of various impurities. Lime nitrogen should be protected from moisture when stored, in order to prevent slow polymerization to dicyanodiamide. It is advisable to use a fresh supply of lime nitrogen for this synthesis.

2. Stirring for one hour in the cold permits the relatively insoluble calcium cyanamide to react with sodium hydroxide and go into solution as sodium cyanamide. If the temperature is not kept below 25° during this time, there is some tendency for polymerization to dicyanodiamide.

3. A good grade of allyl bromide should be used.

4. No allyl bromide is recovered. When water is added to the alcohol distillate, which would undoubtedly contain any unused allyl bromide, none separates. The excess probably reacts to form allyl alcohol. However, no attempt has been made to isolate it.

5. This represents a general procedure for the preparation of dialkyl cyanamides; for example, di-*n*-butyl cyanamide has been prepared in a similar manner, in yields of about 50 per cent of the theoretical amount.

### 3. Other Methods of Preparation

The preparation of diallyl cyanamide by the above method has only recently been described in the literature.[1] However, other dialkyl cyanamides have been prepared by the following methods: the action of chlorocyanogen or bromocyanogen on dialkyl amines;[2] the reaction of dialkyl chloroamines with potassium cyanide;[3] the action of bromine on a mixture of dialkyl amines and potassium cyanide;[4] the action of alkyl halides on disilver cyanamide[5] and on disodium cyanamide.[6] Dimethyl cyanamide has also been prepared by the action of dimethyl sulfate on lime nitrogen[7] and on cyanamide.[8]

[1] J. Am. Chem. Soc. **46**, 1307 (1924); Swiss Pat. 104,101; Ger. Pat. 404,174; Chem. Zentr. **1925, I,** 1242; Versuche mit Diallylderivaten, Dissertation von Paul Graf, Eidgenossischen Technischen Hochschule, Zurich; page 27.

[2] Ann. **90**, 96 (1854); Ber. **32**, 1873 (1899).

[3] Compt. rend. **114**, 483, 1381 (1892); Bull. soc. chim. (3) **7**, 547 (1892); Ann. chim. phys. (7) **3**, 352 (1894).

[4] Compt. rend. **116**, 329 (1893); Bull. soc. chim. (3) **9**, 239 (1893); Am. Chem. J. **36**, 208 (1906).

[5] Ber. **10**, 427 (1877).

[6] Ber. **44**, 3149 (1911).

[7] Ber. **44**, 3150 (1911).

[8] Ber. **44**, 3165 (1911).

XVIII

## 2,3-DIBROMOPROPENE

$$CH_2BrCHBrCH_2Br + NaOH \rightarrow CH_2BrCBr{=}CH_2 + NaBr + H_2O$$

Submitted by R. LESPIEAU and M. BOURGUEL.
Checked by C. S. MARVEL, JOHN R. JOHNSON, and W. L. MCEWEN.

### 1. Procedure

A 500-cc. round-bottom flask is connected by a wide, bent glass tube to an efficient condenser, which is provided with an adapter leading into a 500-cc. receiving flask immersed in an ice bath. Two hundred grams (0.71 mole) of 1, 2, 3-tribromopropane (Note 1) and 10 cc. of water are placed in the reaction flask, and 50 g. (1.25 moles) of sodium hydroxide (Note 2) in small lumps (not pulverized) is added at once with shaking. The mixture warms up and the flask is immediately connected to the apparatus and heated directly by means of a Bunsen burner held in the hand. It is advisable to use a slightly luminous flame about 15 cm. high and to heat with a rotary motion, directing the flame against the sides of the flask.

The mixture is shaken occasionally, and the alkaline layer soon becomes partly emulsified. Heat is applied until vigorous ebullition occurs, whereupon a spontaneous distillation of the reaction product takes place (Note 3). When the reaction slackens, the flask is heated as before. The mass becomes solid as the volatile products are removed. This solid mass which is brownish in color, is heated until no more liquid distils (Note 4). The entire operation up to this point requires twenty to thirty minutes.

The distillate in the receiving flask separates into two layers: an upper layer of water; and a heavy layer of a colorless oil,

consisting of a mixture of 2,3-dibromopropene and unchanged tribromopropane. The distillate is transferred to a 500-cc. separatory funnel and thoroughly agitated with an additional 150 cc. of water (Note 5). The lower layer is decanted and found to weigh 140–145 g. It is subjected to a preliminary distillation under reduced pressure to separate most of the unchanged tribromopropane. All of the material that passes over below 95°/75 mm. consists of 2,3-dibromopropene containing a small amount of water and tribromopropane, and weighs 120–130 g. The residue in the distilling flask consists of unchanged tribromopropane (15–25 g.) (Note 6).

The crude product is dried over calcium chloride and fractionally distilled under reduced pressure (Note 7). The yield of pure, colorless 2,3-dibromopropene boiling at 73–76°/75 mm. is 105–120 g. (74–84 per cent of the theoretical amount). A small quantity of tribromopropane, usually about 5 per cent of the crude material, remains in the distilling flask (Note 6).

## 2. Notes

1. The crude tribromopropane, obtained as described on page 100, may be used without lowering the yield.

2. Potassium hydroxide may be used in place of sodium hydroxide, but it was found that the reaction is much more violent and irregular and the yields are somewhat lower. If potassium hydroxide is used, it is advisable to provide the receiving flask with a reflux condenser to avoid loss when the initial violent reaction occurs. Since the reaction is so rapid, it would be very dangerous to use more than 200 g. of tribromopropane in a single run with potassium hydroxide.

3. In the initial vigorous ebullition, about half of the material distils during a few minutes and it is necessary to wait for this reaction to slacken before continuing to heat the flask. If sodium hydroxide is used, the reaction is vigorous but not violent, and it is possible to use 600 g. of tribromopropane in a 1-l. flask in a single run without danger if the reaction flask is connected with the condenser by means of a wide tube. The yields in larger runs are as good as when smaller runs are made.

4. A small additional quantity of distillate may be obtained by partially evacuating the apparatus, after replacing the adapter and receiving flask by a 250-cc. distilling flask. The amount of material obtained in this way amounts to only 1–2 g. if the reaction flask has been properly heated. It is well to note that flasks which have been repeatedly heated with very strong alkalies become fragile, and care should be used not to reduce the pressure too greatly.

5. The dibromopropene and the wash water have a strong lachrymatory effect and should be manipulated carefully.

6. When a sufficient quantity of these crude residues of tribromopropane has been collected, it may be used for preparing 2,3-dibromopropene. If allowance is made for this recovered material, the yield of 2,3-dibromopropene is 82-87 per cent of the theoretical amount.

7. The separation of 2,3-dibromopropene from tribromopropane is effected easily since their boiling points are quite different.

| Pressure | 2,3-Dibromopropene | Tribromopropane |
|---|---|---|
| 18 mm. | 42– 43° | 101–102° |
| 75 mm. | 75– 76° | 140–142° |
| 760 mm. | 140–143° | 219–221° |

These substances may be distilled under atmospheric pressure with only slight decomposition, but the products become highly colored on standing.

## 3. Other Methods of Preparation

2,3-Dibromopropene has been prepared by the action of potassium [1] or sodium hydroxide [2] on tribromopropane, and by the action of metallic sodium on an ethereal solution of tribromopropane.[3]

[1] Ann. chim. phys. (3) **60**, 42 (1860); (7) **11**, 235 (1897); Ann. **154**, 371 (1870); Ber. **14**, 404 (1881); Bull. soc. chim. (4) **29**, 530 (1921).

[2] Ann. chim. phys. (7) **11**, 235 (1897); Bull. soc. chim. (4) **29**, 530 (1921).

[3] Ann. **156**, 168 (1870).

# XIX

## ETHYL ACETONE DICARBOXYLATE

$$CO_2HCH_2COCH_2CO_2H + 2C_2H_5OH + (HCl) \rightarrow$$
$$CO_2C_2H_5CH_2COCH_2CO_2C_2H_5 + 2H_2O$$

Submitted by ROGER ADAMS and H. M. CHILES.
Checked by H. T. CLARKE and T. F. MURRAY.

### 1. Procedure

THE crude acetone dicarboxylic acid obtained from 700 g. of citric acid, as described on page 5, is treated with 700 g. of absolute ethyl alcohol (Note 1) to which has been added at least 130–150 g. of *dry* hydrogen chloride. The mixture is placed in a flask fitted with a stopper holding a calcium chloride tube and then is heated to 45°. It is kept in a water bath at 45° (bath temperature) with frequent shaking until all of the acid is dissolved (fifteen to twenty minutes). The solution is allowed to cool down to room temperature in the bath and finally to stand about twelve hours (Note 2).

The contents of the flask are then poured into 1300–1400 cc. of ice water, the ester layer separated, and the water-alcohol layer extracted twice with half its volume of benzene (700 cc.). The benzene extracts are added to the original ester, which has been separated. The total solution thus obtained is washed with about 400 cc. of 10 per cent sodium carbonate solution to remove the acid, then once with dilute sulfuric acid, and finally twice with 400 cc. portions of water (Note 3). The benzene is distilled on a water bath, and the ester is distilled under reduced pressure. A small low-boiling fraction comes over first and then the ester, which boils at 131–136°/9–10 mm. or 145–148°/17 mm.

(Note 4). The yield of product amounts to 284–315 g. (42–46 per cent of the theoretical amount based on the citric acid).

## 2. Notes

1. The directions given in the literature call for a smaller amount of alcohol than that given in the procedure but more consistent results were obtained with the method described.

2. The ester should be isolated from the reaction mixture after twelve hours. Longer standing causes a decreased yield.

3. One of the chief precautions which must be observed, if good yields are to be obtained, is thorough and careful washing of the benzene and ester mixture. If this is not done, decomposition occurs during distillation and the yields are lowered by about one-third.

4. The ester must be distilled under low pressure (under 20 mm.) or considerable decomposition occurs.

## 3. Other Methods of Preparation

This ester has been prepared by the esterification of acetone dicarboxylic acid [1] and of ethyl $\gamma$-cyanoacetoacetate.[2]

[1] Ann. **261,** 159 (1891); J. Chem. Soc. **75,** 809 Footnote (1899); **121,** 1642 (1922); Ann. **422,** 6 (1921).

[2] Compt. rend. **111,** 683 (1890).

XX

## ETHYL ORTHOFORMATE

$$2CHCl_3 + 6C_2H_5OH + 6Na \rightarrow 2CH(OC_2H_5)_3 + 6NaCl + 3H_2$$

Submitted by W. E. KAUFMANN and E. E. DREGER.
Checked by F. C. WHITMORE and H. F. HERZOG.

### 1. Procedure

IN a 5-l. round-bottom flask fitted with an 80-cm. reflux condenser, are placed 3 l. of absolute alcohol (Note 1) and 490 g. (4.1 moles) of chloroform (Note 2). The flask is arranged for outside cooling by running water. To the solution, 207 g. (9 moles) of clean sodium cut into pieces which will conveniently drop through the condenser, is added during the course of about two hours. In order to add the sodium at this rate, the flask must be cooled during the addition. When the sodium has entirely reacted and the mixture has been cooled to room temperature, the sodium chloride which has separated is removed by suction filtration with the use of thoroughly dry apparatus (Note 3). The salt is washed on the filter with 200 cc. of absolute alcohol, and the washings are allowed to run into the main filtrate.

The solution is placed in a 3-l. flask fitted with an 80-cm. fractionating column (Note 4) and the excess chloroform and most of the alcohol are distilled off on a steam or water bath. The distillate is caught in a 2-l. suction flask protected from moisture by a drying tube. This distillation requires five or six hours. A mixture of chloroform and alcohol, weighing about 2000 g., is recovered and saved for the next run (Note 3). The liquid remaining in the flask is decanted from the small amount of salt which has separated, into a Claisen flask with a 30-cm. fractionating column (Note 5). The mixture is distilled at atmos-

pheric pressure. The fraction boiling below 85° is mainly alcohol and is discarded. An intermediate fraction of about 100 g., boiling at 85–140°, contains about one-fourth of the total yield. This may be fractionated but is best added to a subsequent run. The orthoformic ester is collected at 140–146° and weighs 120–140 g. (27–31 per cent of the theoretical amount). There is practically no higher-boiling material. Another distillation gives almost all the material boiling over a two-degree range.

After the first run, 400 g. of chloroform and enough absolute alcohol (800–1000 cc.) are added to the recovered chloroform-alcohol mixture to give a total volume of 3 l. The sodium is then added as before. After the excess of chloroform and alcohol has been distilled through the fractionating column, the intermediate fraction from the previous run is added before fractionating. The yield from such a run is about 200 g. (45 per cent of the theoretical amount).

## 2. Notes

1. Good absolute alcohol is essential. The use of alcohol of about 98 per cent gives only about two-thirds the yields obtained with absolute alcohol. Alcohol dried over lime usually runs about 98.5–99.5 per cent. A good method of obtaining a higher grade of absolute alcohol is to treat this alcohol with a little sodium. When the sodium has dissolved, the alcohol is distilled from a steam bath. Under these conditions, any trace of water that may be present on account of the equilibrum

$$C_2H_5OH + NaOH \rightleftarrows C_2H_5ONa + H_2O$$

remains in the concentrated solution of sodium ethylate and sodium hydroxide.

2. Enough chloroform must be used to keep the solution from being alkaline at the end of the reaction.

3. If care is taken to prevent moisture from getting into the recovered alcohol-chloroform mixture, this mixture may be used repeatedly. After it has been used four or five times, the yield begins to fall.

4. The long fractionating column used by Clarke and Rahrs

[Ind. Eng. Chem. 15, 349 (1923)] is a good one for use at this point. If such a column is not available, an 80-cm. reflux condenser without any water in it, may be used, connecting it at the top by means of a wide, bent glass tube to a condenser set downward for distillation.

5. A satisfactory type of flask for the distillation is that illustrated in Org. Syn. 1, 40.

6. The present method is better than that which uses dry ether as a solvent.

7. Yields equally as good as those mentioned in the above procedure are obtained by first preparing a sodium ethylate solution, using the quantities given above and adding this to an alcohol-chloroform solution. One decided disadvantage in this alternative procedure is that, unless a great deal more alcohol is used, the sodium ethylate solution tends to become semi-solid and cannot be introduced easily into the chloroform-alcohol solution. If one attempts to use recovered alcohol, containing chloroform, the sodium chloride which separates as soon as sodium is added, increases the tendency to become semi-solid.

8. The reaction is carried out best without stirring, thus allowing the sodium to float on top. In this way, the hydrogen escapes rapidly and little reduction of the chloroform takes place.

### 3. Other Methods of Preparation

Orthoformic ester has been prepared by the treatment of a mixture of chloroform and alcohol with sodium;[1] by the action of dry sodium ethylate on chloroform[2] or on an ether solution of chloroform;[3] by the action of alcoholic sodium hydroxide on chloroform;[4] and by the action of alcoholic hydrochloric acid on ethyl formimido ester[5] or its mercuric chloride double salt.[6]

[1] Jahresb. **1860**, 390; Ann. **152**, 164 (1869); Ber. **12**, 116 (1879); J. Soc. Chem. Ind. **42**, 430 T (1923).

[2] Ann. **92**, 346 (1854); Z. Chem. **1871**, 186.

[3] Ann. **240**, 103 (1887).

[4] J. prakt. Chem. (2) **48**, 231 (1893).

[5] Ber. **16**, 356 (1883); **31**, 1010 (1898).

[6] Am. Chem. J. **31**, 209 (1904).

Wood and Comley have recently published [7] a method for the preparation of orthoformic ester, in which sodium and chloroform are added alternately to the absolute alcohol. A few runs were made according to their directions but the results were not as satisfactory as those obtained by the procedure given above.

[7] J. Soc. Chem. Ind. **42**, 430 T (1923).

# XXI

## ETHYL OXALATE

$$\begin{array}{l} C(OH)_3 \\ | \\ C(OH)_3 \end{array} \rightarrow \begin{array}{l} CO_2H \\ | \\ CO_2H \end{array} + 2H_2O$$

$$\begin{array}{l} CO_2H \\ | \\ CO_2H \end{array} + 2C_2H_5OH \rightarrow \begin{array}{l} CO_2C_2H_5 \\ | \\ CO_2C_2H_5 \end{array} + 2H_2O$$

Submitted by JOSEPH KENYON.
Checked by C. S. MARVEL and A. B. ADAMS.

### 1. Procedure

IN a large evaporating dish is placed 252 g. (2 moles) of crystalline oxalic acid. The acid is heated on a steam bath for six to eight hours, with occasional stirring, until all the water of crystallization (72 g.) has been expelled. The oxalic acid which is almost anhydrous (weighing approximately 180 g.), is placed in a 1.5-l. round-bottom flask, *A*, containing 500 cc. of absolute alcohol and fitted up as shown in Fig. 1.

The flask *A* is heated by means of an oil bath maintained at 120–125° (Note 1); the mixed vapors of alcohol and water, passing through the fractionating column, are condensed in *D* and the moist alcohol is delivered under the surface of the alcohol contained in flask *B*. In flask *B* are placed 250 cc. of absolute alcohol and about 200 g. of freshly ignited potassium carbonate. Flask *B* is heated in an oil bath maintained at about 95–100°. The moist alcohol delivered to the flask *B* is dried by the potassium carbonate and subsequently returned as vapor under the surface of the liquid in flask *A*. The tube *C*, which is open to the air, acts as a safety valve to the otherwise closed system.

The reaction is run for about five hours. The excess alcohol is then distilled, the residue of ethyl oxalate is distilled under reduced pressure, and the fraction boiling at 98–101°/21 mm. is

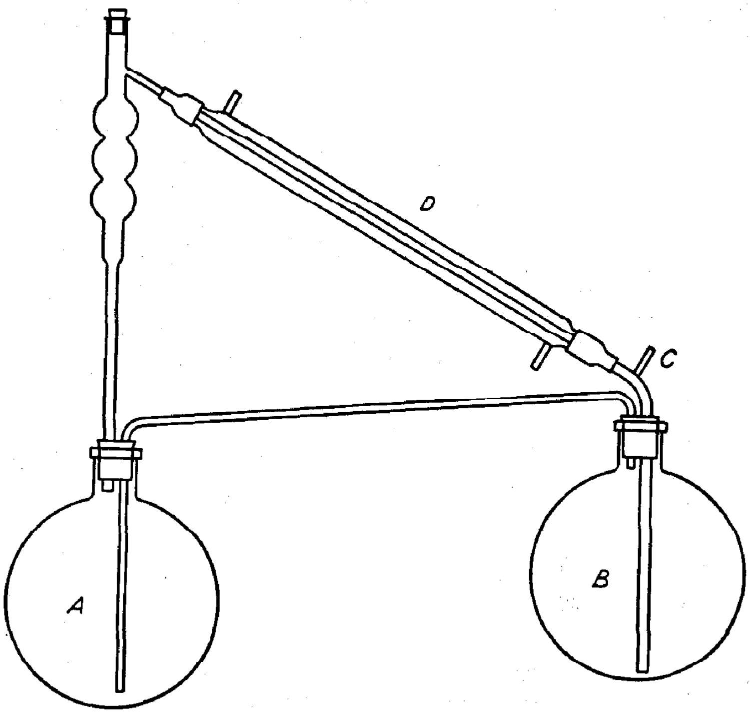



*Fig. 1.*

collected. The yield is 234–264 g. (80–90 per cent of the theoretical amount) (Note 2).

## 2. Notes

1. The temperature varies slightly with the length of the fractionating column. This temperature was noted when an ordinary two-bulb column (about 30 cm. long) was used.

2. A similar procedure may be used for the preparation of methyl oxalate. Instead of distilling this ester, it is better to cool the solution in an ice bath and separate the crystals of

methyl oxalate from the mother liquors in a basket centrifuge. The product thus obtained from 252 g. of crystallized oxalic acid weighs 120–125 g. Upon concentrating the mother liquors, cooling, and again centrifuging the mixture, a further crop of crystals weighing 30–35 g. may be obtained. Thus the total yield of methyl oxalate is 150–160 g. (63–67 per cent of the theoretical amount).

### 3. Other Methods of Preparation

The esterification of oxalic acid by the method of Clarke,[1] in which carbon tetrachloride is used to remove the water from the esterification mixture, is very satisfactory. However, the above procedure, which is based on the method of Frankland and Aston[2] for the preparation of ethyl tartrate, is very easily carried out and the yields are as good as those described by Clarke.

[1] Org. Syn. **2**, 22-26.

[2] J. Chem. Soc. **79**, 517 (1901).

# XXII

## *d*-GLUTAMIC ACID

Hydrolysis of Gluten from Wheat Flour

$$\longrightarrow CO_2HCH_2CH_2CH(NH_2)CO_2H$$

Prepared by H. B. Lewis, H. M. Chiles, and G. J. Cox.
Checked by H. T. Clarke and C. J. Malm.

### 1. Procedure

Four kilos of wheat flour (Note 1) is placed in a large dish and worked with 3000 cc. of water to a stiff dough (twenty minutes). This is allowed to stand fifteen to twenty minutes and then the starch is washed out by gently kneading the dough in running water. The washing is continued until no more starch is carried off by the water and a rubbery mass of gluten, which is no longer sticky, remains. This washing requires twenty-five to thirty-five minutes (Note 2).

The wet gluten (about 1300 g. ) is placed (Note 3) in a 5-l. round-bottom flask and covered with 1600 cc. of concentrated hydrochloric acid (sp. gr. 1.19). This reaction mixture is then warmed on the steam bath until the purple color disappears (about two hours). A reflux condenser is then attached and the solution is boiled gently over a flame for about eighteen hours. The hot solution is filtered with suction (Note 4) and the black residue of melanin is washed with about 200 cc. of water. The combined filtrate and washings are concentrated under reduced pressure until the volume is reduced to about 1500 cc. This solution is allowed to cool to room temperature and the crystals of glutamic acid hydrochloride filtered and washed with two 30-cc. portions of 95 per cent ethyl alcohol saturated with hydrogen chloride. The washings are discarded (Note 5) and the

mother liquor is concentrated to 500–600 cc. under reduced pressure; the second crop of crystals obtained on cooling is washed as before. The mother liquor is chilled in an ice-salt bath and saturated with hydrogen chloride; after standing over night in the ice-box, the crystals are filtered and washed as were the previous crops.

The combined crops of crystals are dissolved in the smallest possible amount of hot water (400–500 cc.). The solution is heated on a steam bath for about ten minutes, with 10 g. of decolorizing carbon (Norit) and filtered, whereupon a pale yellow solution is obtained (Note 6). The pure glutamic acid hydrochloride is again precipitated by saturating the ice-cold solution with hydrogen chloride and allowing it to stand over night in an ice-box. This crop of crystals is filtered and washed as before with alcoholic hydrogen chloride and finally with two 200-cc. portions of ether. On drying, 110–120 g. of glutamic acid hydrochloride is obtained. The mother liquor is concentrated to 250–300 cc. and saturated with hydrogen chloride, whereupon another crop of crystals weighing 25–50 g. is obtained (Note 7). The total yield is 140–145 g. The product melts at 202–204° on rapid heating (Note 8).

In order to obtain free glutamic acid, 183 g. (1 mole) of the above hydrochloride is dissolved in 750 cc. of distilled water and treated with 500 cc. of 2 N sodium carbonate solution. After standing over night, the free acid which has crystallized is filtered and washed with ice water until free of sodium chloride. The mother liquor and washings are united and concentrated to 300–350 cc. and again allowed to stand over night. The crystals so obtained are filtered and washed with ice-water. The total yield of colorless crystals which melt at 197–198° (corr.) is 109–120 g. (74–82 per cent of the theoretical amount).

## 2. Notes

1. The yield of glutamic acid hydrochloride varies somewhat with the brand of flour. The results described in this procedure were obtained with Gold Medal flour.

2. The water should have a temperatue of 20–25° in order to avoid unduly chilling the hands. Instead of washing the starch out of the gluten as described in the procedure, it is sometimes found convenient to place the flour in a muslin sack and wash the starch out through the meshes. This procedure usually requires a somewhat longer time.

3. The gluten is best introduced by first replacing all the air in the flask by steam, and then allowing the suction caused by the condensation of the steam to draw in the mass in one portion.

4. The filtrations are best made by using "filtros" plates. If ordinary filter paper is employed, at least three thicknesses must be used to prevent the acid solution from eating through the paper during the filtration.

5. The alcoholic washings contain much colored matter, and must not be added to the mother liquors.

6. The one treatment with decolorizing carbon should be sufficient if the operations have been carried out correctly. If not, several subsequent treatments may be necessary, in which case several short periods of treatment with small quantities give the best results. Continued heating with a large sample of bone-black is apt to deepen the color.

7. If the mother liquors are further concentrated, ammonium chloride separates; it is therefore advisable to discard them at this point.

8. If gluten flour (40 per cent gluten) is used instead of ordinary flour, the procedure is approximately the same. A 5-lb. sack* of gluten flour is washed to remove the starch. The wet gluten is placed in a 6-l. Pyrex flask with 3500 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and the hydrolysis is carried out as described above. After the hydrolysis and removal of the melanin by filtration, the solution is concentrated to about 1300 cc. The glutamic acid hydrochloride is then precipitated as already described. After two recrystallizations, the yield is 180–190 g. From the mother liquors a further yield of 45–50 g. is obtained, making a total of 225–230 g.

* This is the size of the sacks that are commonly obtained on the market.

"Glidine," a commercial diabetic food which is prepared from wheat flour and contains over 90 per cent of protein, may be used as a satisfactory source of glutamic acid. If this is used, it is not necessary to wash in order to remove the starch. From 1130 g. of this material, by hydrolyzing with 2500 cc. of concentrated hydrochloric acid and working up as before, 275–285 g. of glutamic acid hydrochloride may be obtained. Usually, the product from glidine is more difficult to decolorize. It has been found that an ether extraction of the hydrolysis mixture, after removal of the melanin, improves the color of the final product.

Glutamic acid may also be obtained from "Ajinomoto,"* a Japanese food product in powder form, consisting mainly of the monosodium salt of glutamic acid. The exact amount of this constituent may be determined by the Van Slyke amino nitrogen method or by igniting a sample of the material in a platinum crucible and titrating the residue of sodium carbonate. The calculated quantity of normal hydrochloric acid is added to a solution of the Ajinomoto in four times its weight of water, and then the solution is boiled with a little decolorizing carbon and filtered hot; the clear solution is allowed to stand over night in the ice-box and the crystallized glutamic acid is filtered and washed with ice-water. In this way, 72–73 per cent of the theoretical amount can be obtained; thus, 100 g. of Ajinomoto, found to contain 84 g. of monosodium glutamate, was dissolved in 400 cc. of water and treated with 500 cc. of normal hydrochloric acid and 54–55 g. of pure glutamic acid was obtained.

### 3. Other Methods of Preparation

*d*-Glutamic acid hydrochloride has been obtained by the hydrolysis of a large number of proteins. The common protein used in its preparation is gliadin from wheat.[1] Casein has also

* Ajinomoto may be obtained from S. Suzuki and Co., New York City.

[1] Abderhalden, Handbuch der Biochem. Arbeitsmethoden, **2**, 492 (1910); Ger. Pat. 301,499; Frdl. **13**, 202 (1917); Brit. Pat. 106,081; C. A. **11**, 3042 (1917); U. S. Pat. 1,255,390; C. A. **12**, 909 (1918); J. Am. Chem. Soc. **44**, 1801 (1922).

been recommended.[2] In general, the above procedure is like those already described in the literature but many details have been added.

*d*-Glutamic acid has been prepared from the hydrochloride by treating a water solution with strong alkalies,[2] alkali carbonates,[3] and ammonium hydroxide.[4] Hopkins[5] has shown that the addition of 6–8 volumes of alcohol to a concentrated water solution of glutamic acid hydrochloride will cause a slow precipitation of the free amino acid.

The preparation of *d*-glutamic acid from Ajinomoto was first described by Schmidt and Foster.[6] This is a very convenient method, but is more expensive than the preparation from flour.

[2] J. Am. Chem. Soc. **39**, 1429 (1917).

[3] Ger. Pat. 301,499; Frdl. **13**, 202 (1917); Brit. Pat. 106,081; C. A. **11**, 3042 (1917).

[4] Z. physiol. Chem. **77**, 76 (1912).

[5] Biochem. J. **15**, 293 (1921).

[6] Proc. Soc. Exptl. Biol. Med. **18**, 205 (1921).

XXIII

# GLUTARIC ACID

$$CNCH_2CH_2CH_2CN + 2HCl + 4H_2O \rightarrow$$
$$CO_2HCH_2CH_2CH_2CO_2H + 2NH_4C$$

Submitted by C. S. MARVEL and W. F. TULEY.
Checked by H. T. CLARKE and E. E. DREGER.

## 1. Procedure

IN a 2-l. round-bottom flask are placed 100 g. (1.06 moles) of trimethylene cyanide (p. 103) and 500 g. (4.8 moles) of hydrochloric acid (sp. gr. 1.18). The mixture is refluxed for about four hours and then the solution is evaporated to dryness, preferably under reduced pressure. The dry residue, consisting of ammonium chloride and glutaric acid, is extracted with about 300 cc. of boiling ether. The ether solution is filtered and the residue is further extracted with two 100 cc. portions of boiling ether. The combined ether extracts containing the glutaric acid are evaporated (Note 1) to about 150–200 cc., whereupon the acid begins to crystallize. Then a liter of benzene (Note 2) is added and the mixture is heated until the glutaric acid dissolves. On cooling in an ice-salt bath, the acid crystallizes. The first crop weighs 103–105 g. (Note 3). The filtrate is concentrated to about one-third its original volume and cooled, whereupon a second crop of 13–14 g. of pure glutaric acid is obtained. The total yield is thus 116–119 g. (83–85 per cent of the theoretical amount) of a product melting at 97–98°.

## 2. Notes

1. Most of the ether can be recovered by concentrating the solution in a flask attached to a condenser set for distillation.

2. The glutaric acid may be directly extracted from the ammonium chloride with benzene, but this is less satisfactory on a small scale than is the procedure given.

3. When the benzene solution is chilled to 0° or lower, almost all of the glutaric acid separates in the first crop of crystals.

## 3. Other Methods of Preparation

Many methods have been mentioned in the literature for the preparation of glutaric acid. Of these, the only methods of preparative interest are: the hydrolysis of trimethylene cyanide with acids or alkalies,[1] the hydrolysis of methylene dimalonic ester[2] or methylene dicyanoacetic ester,[3] and the oxidation of cyclopentanone with nitric acid.[4] In this country the cheapness of trimethylene glycol makes it the best source for glutaric acid. The method described in the procedure is a modification of that originally described by Reboul.[5]

[1] Compt. rend. **82,** 1197 (1876); Ann. **182,** 341 (1876); Ann. chim. phys. (5), **14,** 501 (1878).

[2] Ber. **19,** 1055 (1886); **27,** 2346 (1894); Bull. soc. chim. (4) **11,** 382 (1912).

[3] J. Chem. Soc. **89,** 1460 (1906).

[4] Ann. **275,** 315 (1893).

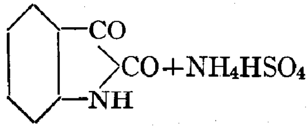
[5] Compt. rend. **82,** 1197 (1876).

# XXIV

## ISATIN

$$C_6H_5NH_2 + NH_2OH + CCl_3CH(OH)_2 \rightarrow C_6H_5NHCOCH{=}NOH + 3HCl + H_2O$$

$$C_6H_5NHCOCH{=}NOH + H_2SO_4 \rightarrow$$



Submitted by C. S. MARVEL and G. S. HIERS.
Checked by J. B. CONANT.

### 1. Procedure

A. *Isonitrosoacetanilide.* In a 5-l. round-bottom flask are placed 90 g. (0.54 moles) of chloral hydrate and 1200 cc. of water. To this solution are then added, in order: 1300 g. of crystallized sodium sulfate (Note 1); a solution of 46.5 g. (0.5 moles) of aniline (Note 2) in 300 cc. of water to which 43 cc. (0.52 mole) of concentrated hydrochloric acid (sp. gr. 1.19) has been added to dissolve the amine (Note 3); and, finally, a solution of 110 g. (1.58 moles) of hydroxylamine hydrochloride (Note 4) in 500 cc. of water. The flask is heated over a wire gauze by a Meker burner so that vigorous boiling begins in about forty to forty-five minutes. After one to two minutes (Note 5) of vigorous boiling the reaction is complete. During the heating period, some crystals of isonitrosoacetanilide separate. On cooling the solution in running water the remainder crystallizes, is filtered with suction, and air-dried. The yield is 65–75 g. (80–91 per cent of the theoretical amount) of a product melting at 175°.

B. *Isatin.* Six hundred grams of concentrated sulfuric acid (sp. gr. 1.84) is warmed to 50° in a 1-l. round-bottom flask

fitted with an efficient mechanical stirrer and to this, 75 g. of dry (Note 6) isonitrosoacetanilide is added at such a rate as to keep the temperature between 60–70° but not higher (Note 7). External cooling should be applied at this stage so that the reaction can be carried out more rapidly. After the addition of the isonitroso compound is finished, the solution is heated to 80° and kept at this temperature for about ten minutes to complete the reaction. Then the reaction mixture is cooled to room temperature and poured upon ten to twelve times its volume of cracked ice. After standing for about one-half hour, the isatin is filtered with suction, washed several times with cold water to remove the sulfuric acid, and then dried in the air. The yield of crude isatin, which melts at 189–192°, is 47–52 g. (71–78 per cent of the theoretical amount). This product is pure enough for many purposes.

For purification, 200 g. of the crude product is suspended in 1 l. of hot water and treated with a solution of 88 g. of sodium hydroxide in 200 cc. of water. The solution is stirred mechanically and the isatin passes into solution. Dilute hydrochloric acid is then added, with stirring, until a slight precipitate appears. This requires about 290–300 cc. of an acid made by diluting one volume of concentrated hydrochloric acid (sp. gr. 1.19) with two volumes of water (Note 8). The mixture is then filtered at once, the precipitate is rejected, and the filtrate is made acid to Congo red paper with hydrochloric acid. The solution is then cooled rapidly and the isatin which separates is filtered with suction and dried in the air. The pure product thus obtained weighs 150–170 g. (Notes 9 and 10) and melts at 197–200° (corr.)

Isatin may also be crystallized from three times its weight of glacial acetic acid. In this case it is obtained in large brown-red crystals which melt at 196–197°.

## 2. Notes

1. Several runs were made in which the amounts of water and sodium sulfate were varied over a considerable range and this concentration was found to give the best yield of product of

good quality. The sodium sulfate seems to have more than a salting-out effect. If a saturated solution of sodium chloride is used no product is obtained.

2. Redistilled aniline boiling over a two-degree range was used in these experiments. The ordinary "pure" grade gives slightly lower yields.

3. If the aniline is not in solution, a considerable quantity of tarry material is formed during the heating period. No tar is formed when the method described is used.

4. The hydroxylamine hydrochloride used was the crude material prepared as described in Org. Syn. **3**, 61. Preliminary experiments showed that this reagent must be present in considerable excess. Equally good results were obtained by using a solution of crude hydroxylamine sulfate which also contained sodium sulfate and ammonium sulfate with a little excess sulfuric acid. The hydroxylamine content was determined in this solution by titration with potassium permanganate solution. When this crude solution is used, the addition of sodium sulfate is not always necessary.

5. Longer heating of the reaction mixture gives a lower yield of dark-colored product.

6. If too much moisture is left in the isonitrosoacetanilide it is not easy to control the reaction with sulfuric acid.

7. The reaction does not start below 45–50° but becomes too violent above 75–80°. If the temperature becomes too high, the entire run is lost by charring. Stirring is needed to prevent local overheating.

8. The correct amount of acid that must be added to precipitate the impurities but not the isatin, will vary with different samples of crude isatin. If too much acid is added, some isatin comes down with the impurities. This may be saved and added to a subsequent run.

9. The yield of isatin is lower than for some of its derivatives. The explanation given in the literature is that some sulfonation occurs during the treatment with sulfuric acid, with corresponding loss of product.

10. This method can be applied successfully to other isatin

derivatives. Thus, under the same conditions, 54 g. of *p*-toluidine gives 75–77 g. (93–96 per cent of the theoretical amount) of isonitrosoaceto-*p*-toluidine melting at 162°. Eighty grams of this isonitroso compound treated as described under isonitrosoacetanilide, gives 65–68 g. (90–95 per cent of the theoretical amount) of crude 5-methyl isatin melting at 179–183°. This is purified as described under isatin by solution in sodium hydroxide and partial neutralization to throw out the impurities or by recrystallization from three parts of glacial acetic acid. The purified 5-methyl isatin melts at 187°.

## 3. Other Methods of Preparation

There are only two practical laboratory methods for the production of isatin, viz.: the oxidation of indigo,[1] and the condensation of aniline, chloral hydrate, and hydroxylamine salts, followed by the action of sulfuric acid.[2]

Of these methods, that of Sandmeyer[2] using aniline, chloral hydrate, and hydroxylamine salts, seemed most promising and has been studied in detail. The present method differs from that described by Sandmeyer in the use of hydroxylamine hydrochloride instead of a crude solution of hydroxylamine sulfate, and in the use of sodium sulfate to salt out the isonitroso compound.

[1] J. prakt. Chem. **24**, 11 (1841); **25**, 434 (1842); **95**, 177 (1865); **97**, 86 (1866); (2) **43**, 211 (1891); Ann. **53**, 10 (1845); **190**, 369 (1878); Jahresb. **1865**, 580; Ber. **17**, 976 (1884); Ger. Pat. 229,815; Frdl. **10**, 353 (1910).

[2] Helvetica Chim. Acta **2**, 237, 239 (1919); Brit. Pat. 128,122; C. A. **13**, 2375 (1919).

# XXV

## *dl*-METHYL ETHYL ACETIC ACID

$$C_2H_5CHBrCH_3 + Mg \rightarrow C_2H_5CH(MgBr)CH_3$$
$$C_2H_5CH(MgBr)CH_3 + CO_2 \rightarrow C_2H_5CH(CO_2MgBr)CH_3$$
$$C_2H_5CH(CO_2MgBr)CH_3 + H_2O \rightarrow C_2H_5CH(CO_2H)CH_3 + Mg(OH)Br$$

Submitted by HENRY GILMAN and H. H. PARKER
Checked by H. T. CLARKE and M. R. BRETHEN.

### 1. Procedure

IN a 2-l. three-necked flask, fitted with a mechanical stirrer, condenser, thermometer well, and 500-cc. separatory funnel, is placed 48 g. (2 moles) of magnesium shavings. The shavings are then covered with 200 cc. of anhydrous ether. A solution of 274 g. (2 moles) of secondary butyl bromide (Note 1) in 300 cc. of anhydrous ether is dropped slowly on to the magnesium. Only a small amount should be added before the reaction starts. The well-stirred mixture is allowed to remain at room temperature during the addition which requires from two to three hours. When the secondary butyl bromide has all been added, the reaction is practically complete and further stirring or refluxing is unnecessary. An additional 500 cc. of anhydrous ether is added.

The reaction flask is then surrounded by an ice and salt mixture, and carbon dioxide is introduced above the surface with stirring. The rate of flow is regulated so that the temperature of the reaction mixture does not rise above $+2°$. The gas, obtained directly from a cylinder, is dried by passing through two wash bottles containing concentrated sulfuric acid and is admitted to the flask through an entry tube 10 mm. in diameter, at a height

of about 25 mm. above the surface of the ether solution (Note 2). The time required for the completion of the reaction varies from one to two hours. When the reaction is complete, the temperature falls below $-5^\circ$ and does not rise on increasing the rate of flow of carbon dioxide.

The reaction mixture is then hydrolyzed in the flask with 25 per cent sulfuric acid (Note 3). Cooling the solution with ice and water permits of rapid hydrolysis without danger of loss of the material through too vigorous refluxing. The mixture is transferred to a 2-l. separatory funnel and the ether layer separated. The water layer is extracted with three 100-cc. portions of ether. The combined ether extracts are washed with 25 per cent sodium hydroxide solution until all of the organic acid is converted to the salt and thus removed (Notes 4 and 5). About 300 cc. of the sodium hydroxide solution is required.

The alkaline extract is distilled to remove ether and other volatile impurities. It is then acidified with concentrated hydrochloric acid and the acid layer separated. The water layer is distilled from a 2-l. flask until no more oily acid comes over (Note 6). The distillate is saturated with salt and the acid layer separated. This water layer, together with the low-boiling fraction from the acid distillation, is distilled, and the distillate salted out as before.

The combined acid layers are placed in a 250-cc. distilling flask connected to an air condenser, which is in turn connected to a water condenser. This arrangement permits of very rapid distillation of the product which is collected at 173–175°. The yield of acid is 135–136 g. (66–67 per cent of the theoretical amount based on the quantity of secondary butyl bromide used) (Note 7).

## 2. Notes

1. The secondary butyl bromide must be of high purity. It may be prepared by the general method of preparing alkyl bromides, described in Org. Syn. 1, 1. Secondary butyl alcohol may be obtained from the Standard Oil Co. of New Jersey.

2. Troublesome clogging of the tube is avoided by having it above the solution instead of immersed in it.

3. The reaction product solidifies if it is allowed to stand too long in the reaction flask, thus causing difficulty with the hydrolysis. Time will be saved if the acid is added immediately after the addition of the carbon dioxide is completed. A rather concentrated acid solution is used in order to keep the volume of the water layer as small as possible.

4. The products of the reaction cannot be separated smoothly by fractional distillation prior to the extraction with alkali.

5. Considerable heat is evolved in the neutralization of the acid with the sodium hydroxide. The extraction can be carried on faster and without loss if the solution is cooled by the direct addition of ice. It is convenient to test the extracts with phenolphthalein to determine when all of the acid has been removed.

6. The methyl ethyl acetic acid may also be obtained by extraction of the acidified solution with ether. This method is not recommended, as small amounts of alcohol which are invariably present in this solvent, contaminate the product by the formation of the ethyl ester.

7. By the same general method, *n*-butyl bromide gives *n*-valeric acid in 64–65 per cent yield, bromobenzene gives benzoic acid in 70–71 per cent yield, and cyclohexyl bromide gives hexahydrobenzoic acid in 68 per cent yield.

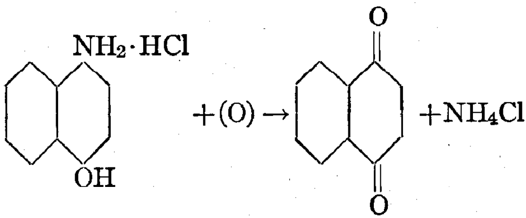
### 3. Other Methods of Preparation

*dl*-Methyl ethyl acetic acid may be prepared from methyl ethyl malonic ester by hydrolysis and subsequent heating of the methyl ethyl malonic acid.[1] The yield by this method, in the preparation of large quantities, is about 61 per cent of the theoretical amount based on the malonic ester used. The acid was first prepared by Saur[2] from methyl ethyl acetoacetic ester. It has also been made by oxidation of the corresponding aldehyde with chromic acid.[3]

[1] Ann. **298**, 167 (1897).
[2] Ann. **188**, 257 (1877).
[3] Monatsh. **7**, 56 (1886).

XXVI

## 1,4-NAPHTHOQUINONE



Submitted by J. B. Conant and S. A. Freeman.
Checked by Henry Gilman and C. E. Adams.

### 1. Procedure

In a 5-l. round-bottom flask are placed 180 g. (0.92 mole) of 1,4-aminonaphthol hydrochloride (Note 1), 20 g. of sodium bisulfite, and 2.5 l. of water. The mixture is heated over a ring burner until it just begins to boil and the resulting dark solution is filtered through a fluted filter paper in a 15-cm. glass funnel. When the filtrate has cooled to 55–65°, it is poured through a fluted filter into a solution of 135 g. (0.45 mole) of sodium dichromate, 140 cc. (2.5 moles) of concentrated sulfuric acid, and 300 cc. of water, in an 8-l. earthenware crock. The temperature of the acidified dichromate solution should be 40–50°; the addition of the sulfuric acid liberates enough heat to raise the temperature to this point. The solution is stirred by hand as the amine hydrochloride is added; a brown precipitate of the quinone forms immediately and the temperature rises somewhat (Note 2). The mixture is allowed to stand three hours and then is transferred to two 2-l. beakers, cooled in an ice bath to 10°, and filtered through a 15-cm. Büchner funnel. The precipitate

is washed with 1 l. of cold water in several small portions. The crude quinone thus obtained, when dried in the air, weighs 105–120 g. (71–82 per cent of the theoretical amount based on the aminonaphthol hydrochloride). It is crystalline and light brown in color (m.p. 120–123°) (Note 3).

The purification of the crude quinone is accomplished by sublimation in a current of steam under diminished pressure (Note 3). A 2-l. round-bottom short-neck flask is immersed as

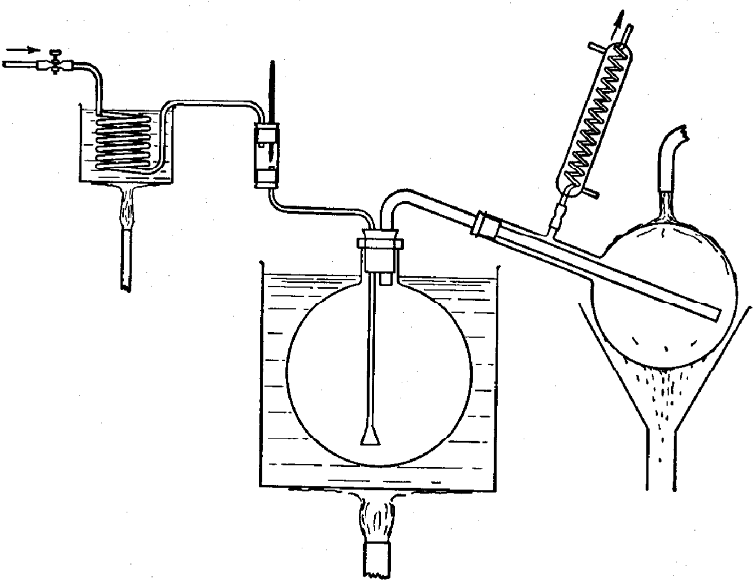


*Fig. 2.*

completely as possible in an oil bath (See Fig. 2). A rubber stopper carries a steam inlet of 5-mm. glass tubing, flared at the end and extending nearly to the bottom of the flask. A "goose-neck" of 20-mm. glass tubing is fitted into another opening in the stopper and extends well into the middle of the receiving flask, which is a 1-l. round-bottom distilling flask with the side tube pointing upwards and attached to a condenser. The flask is well cooled by running water. Dry steam is admitted into the apparatus through a piece of rubber suction tubing carrying a

screw pinchcock; the steam passes through two feet of lead tubing immersed in an oil bath, then through a tube carrying a thermometer (to record the temperature of the entering steam), and then directly into the flask (Note 4). The crude quinone from one run is made into a thin paste with a 10 per cent solution of calcium chloride, 15–20 cc. of solution being used for each 10 g. of quinone (Note 5). The paste is then introduced into the 2-l. flask which is rotated so that its entire inner surface is coated. The flask is placed in the oil bath which has been heated to 100°, the apparatus connected, and the temperature of the bath raised to 115–120°. The pressure is cautiously lowered by opening the connection to the suction. When all the water has evaporated from the flask, superheated steam at a temperature of 130° is admitted at such a rate that the distillate is adequately condensed. The pressure should be about 20 mm. The oil bath used for superheating the steam is kept at 200–220°, the temperature being controlled by the temperature of the thermometer in the steam. The quinone volatilizes rapidly and collects in the condenser. From time to time, the process is interrupted to empty the receiver; the distillation is continued until no more quinone distils. The distillate is filtered with suction and the quinone dried at room temperature in the air or under reduced pressure. The yield of pure quinone is 73–85 g. (50–58 per cent of the theoretical amount based on the amine hydrochloride). The pure quinone is lemon-yellow and melts at 123–124°.

## 2. Notes

1. The aminonaphthol hydrochloride (Org. Syn. 3, 7) need not be dried before using; the directions as here written correspond to the average yield from 200 g. of alpha-naphthol. The free base is unstable in solution, being easily oxidized by the air; the presence of bisulfite decreases this tendency.

2. The oxidation is carried out in warm solution to prevent the separation of the aminonaphthol hydrochloride on cooling. However, if the temperature is too high (above 85°) a black product is obtained.

3. The crude quinone thus obtained is light brown; the shade

varies somewhat with the experiment. It is about 80–90 per cent pure as determined by electrometric titration, and would be suitable for many purposes. It can be further purified by crystallization from benzene or ligroin. This is a difficult procedure, however, and always yields a light brown product and not the lemon-yellow material obtained by sublimation. Whether or not the difference in color is due to an impurity not removed by crystallization has not been determined.

4. If a considerable quantity of the quinone is to be purified, it is desirable to set up a superheating device made entirely of lead tubing and thus do away with the glass and rubber connections. The lead coil is made of 6-mm. lead tubing and is soldered by a T-joint on to a piece of 12-mm. lead tubing, which carries an opening for the thermometer at the top. The lower end of this tube is soldered to 10-mm. lead tubing which leads the steam into the flask arranged for the distillation.

5. The use of calcium chloride as a "binder" is necessary to prevent the crude quinone from being blown over with the steam. The temperature of the bath must not exceed 125°, as a very rapid decomposition occurs above this point. The speed of this rather troublesome purification process depends primarily on the surface exposed in the flask, provided this surface is in fairly good thermal equilibrium with the oil bath. Five to eight hours will usually be required for the sublimation of the amounts given in the directions.

## 3. Other Methods of Preparation

1,4-Naphthoquinone has been prepared by the oxidation of naphthalene,[1] 1,4-aminonaphthol,[2] 1,4-naphthylene diamine,[2] and 1,4-naphthylamine sulfonic acid.[3] Recent work[4] has shown that the oxidation of the 1,4-aminonaphthol is the most convenient method of preparation.

[1] Ann. **167**, 357 (1873); J. Chem. Soc. **37**, 634 (1880); **39**, 220 (1881). J. Russ. Phys. Chem. Soc. **16**, 417 (1884).

[2] Ann. **183**, 242 (1876); **286**, 70 (1895); Ber. **14**, 1796 (1881); J. prakt. Chem. (2) **62**, 31 (1900); J. Am. Chem. Soc. **46**, 1862 (1924).

[3] Ber. **12**, 2306 (1879).

[4] J. Am. Chem. Soc. **46**, 1862 (1924).

## *m*-NITROCINNAMIC ACID

$$(m)\ NO_2C_6H_5CHO + CH_3CO_2Na + (CH_3CO)_2O \rightarrow$$
$$(m)\ NO_2C_6H_4CH{=}CHCO_2H + CH_3CO_2H + CH_3CO_2Na$$

Submitted by F. K. Thayer.
Checked by Roger Adams and A. B. Adams.

### 1. Procedure

In a 200-cc. round-bottom flask, fitted with a reflux condenser, are placed 50 g. (0.33 mole) of *m*-nitrobenzaldehyde (Note 1), 40 g. (0.48 mole) of freshly fused sodium acetate, and 70 g. (0.68 mole) of acetic anhydride. The contents of the flask are well mixed and the mixture heated in an oil bath held at 180° for about thirteen hours. After the reaction product has been allowed to cool slightly, it is poured into 200–300 cc. of water and then filtered by suction (Note 2). After the solid has been washed several times with water, it is dissolved in a solution of 20 cc. of ammonium hydroxide (sp. gr. 0.9) in about 200 cc. of water. The solution of the ammonium salt, after filtering, is poured into a solution of 15 cc. of sulfuric acid (sp. gr. 1.84) in about 200 cc. of water (Note 3). The precipitated *m*-nitrocinnamic acid is filtered, redissolved in ammonium hydroxide, and again precipitated by pouring the solution into dilute sulfuric acid (Note 4).

After the last precipitation, the *m*-nitrocinnamic acid is washed with a little water and then sucked as dry as possible (Note 5). The product, which still contains considerable water, is dissolved in 250–300 cc. of boiling 95 per cent alcohol from which the nitrocinnamic acid crystallizes on cooling. The yield amounts to 47–49 g. (74–77 per cent of the theoretical amount).

The product is pale yellow and melts at 192–194°. If a purer product is desired, it may be recrystallized from benzene or alcohol (Note 6).

## 2. Notes

1. The *m*-nitrobenzaldehyde used was the technical grade and melted at 50–53°.

2. In one run, the product was extracted from the reaction mixture with benzene, removed from the benzene by a sodium carbonate solution, and this solution in turn acidified to obtain the *m*-nitrocinnamic acid. Neither the product nor the yield was as satisfactory by this method.

3. If acid is added to the solution of the ammonium salt, the precipitated *m*-nitrocinnamic acid carries down a considerable quantity of ammonium salts.

4. There is always a small amount of material that is insoluble in the ammonium hydroxide. This is removed by the second treatment.

5. The product is very difficult to dry. If it is removed from the filter after washing, several days are required for it to become dry. This dry product melts at about 190–193°.

6. The melting point of *m*-nitrocinnamic acid is given in the literature as 195° and 196–197°. Beilstein describes it as yellow needles. Alcohol is mentioned as a good solvent for recrystallization but experience in this work showed that benzene is also satisfactory, a white *m*-nitrocinnamic acid being obtained from this solvent.

## 3. Other Methods of Preparation

*m*-Nitrocinnamic acid has been prepared by the condensation of *m*-nitrobenzaldehyde with malonic acid in the presence of bases such as aniline and ammonia.[1] The best yield reported by this process is 72 per cent.

In the preparation from *m*-nitrobenzaldehyde, sodium acetate, and acetic anhydride,[2] no yield is mentioned in the literature.

[1] Ber. **31**, 2610 (1898).

[2] Ber. **11**, 1782 (1878); **13**, 2060 (1880); **46**, 3732 (1913); J. prakt. Chem. (2) **82**, 425 (1910).

XXVIII

# NITROUREA

$$NH_2CONH_2 \cdot HNO_3 + (H_2SO_4) \rightarrow NH_2CONHNO_2 + H_2O$$

Submitted by A. W. INGERSOLL and B. F. ARMENDT.
Checked by HENRY GILMAN and C. C. VERNON.

## 1. Procedure

IN a 2-l. Erlenmeyer flask provided with a mechanical stirrer and thermometer, and surrounded by an ice-salt mixture, is placed 700 cc. of concentrated sulfuric acid. The stirrer is started, and when the acid is cooled to $-3°$ or below, 200 g. of dry, powdered urea nitrate is added in small portions at such a rate that the temperature does not rise above $0°$. The addition will require about one-half hour. Stirring is continued for another half hour, the temperature being kept below $+3°$ (Note 1). Then the mixture is poured upon 1000 g. of ice.

The white, finely divided precipitate of nitrourea is filtered upon a 12-cm. Büchner funnel. A hardened filter paper (Note 2) is used in this operation and the nitrourea is pressed as dry as possible. The product is washed in the funnel with four portions of cold water just sufficient to cover it and pressed dry each time (Note 3). Then it is dried in the air (Note 4). By strongly cooling the filtrates, a further small amount of nitrourea may be obtained and added to the main portion. The yield of air-dried material is 120–150 g. (70–87 per cent of the theoretical amount). It melts with decomposition at 150–164° and is sufficiently pure for use in the preparation of semicarbazide (Note 5).

## 2. Notes

1. If bubbles of gas begin to be evolved while stirring, the mixture should be poured at once upon ice.

2. A hardened filter is necessary. Whatman's No. 50 is satisfactory.

3. Cracks appear when the nitrourea is filtered; hence, care must be taken that the water used for washing does not go through the cracks instead of through the material. If desired, the nitrourea may be removed from the funnel, made into a paste with about 800 cc. of cold water, and again filtered.

4. The product may be dried on a steam plate if the heating is not continued too long.

5. Various samples of nitrourea prepared in this way melt differently and therefore the melting point is not a suitable indication of purity. A uniform product can also be obtained by crystallizing half of the crude material obtained in one run from 1 l. of water at a temperature not over 55°, and using the filtrate to crystallize the second half. Even this recrystallized material does not have a definite melting point.

## 3. Other Methods of Preparation

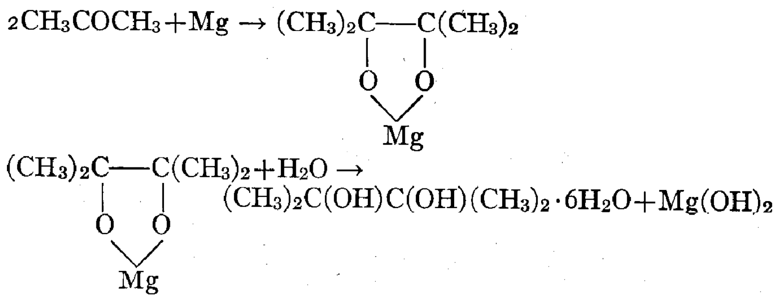
Nitrourea has been made only by the action of concentrated sulfuric upon urea nitrate.[1] The procedure given above is essentially the same as that originally published by Thiele and Lachman.[2]

[1] Ann. **288**, 281 (1895); Rec. trav. chim. **31**, 21 (1912).

[2] Ann. **288**, 281 (1895).

## XXIX

# PINACOL HYDRATE





Submitted by ROGER ADAMS and E. W. ADAMS.
Checked by H. T. CLARKE and ROSS PHILLIPS.


## 1. Procedure

IN a 5-l. round-bottom flask, fitted with a stopper holding a separatory funnel and an efficient reflux condenser (Note 1) closed at the top with a calcium chloride tube (Note 2), are placed 80 g. (3.29 moles) of magnesium turnings and 800 cc. of dry benzene (Note 3). Through the dropping funnel is added gradually a solution of 90 g. of mercuric chloride in 400 g. (6.9 moles) of acetone (Note 4), carefully at first and then more rapidly after the reaction starts. The time of addition is about five to ten minutes (Note 5). Sometimes the reaction does not commence until a considerable proportion of the acetone solution of mercuric chloride has been added. In this case the reaction proceeds very vigorously when it does start and the flask must be cooled in running water to avoid loss through the condenser. As soon as the first vigorous reaction is over, a mixture of 200 g. (3.45 moles) of acetone and 200 cc. of benzene is added (Note 6). When the reaction slows down, the flask is heated on a water bath until no further reaction is evident (about two hours). During this time the magnesium pinacolate swells until it fills

the flask about three-quarters full. The flask is removed from the condenser and shaken until the reaction mass is well broken up (Note 7). The condenser is again attached and the heating continued for another hour.

Through the separatory funnel is then added 200 cc. of water and the reaction mixture is heated another hour. The flask should be shaken occasionally during this time. The reaction mixture is cooled to about 50° and filtered. The solid is returned to the flask and heated for ten minutes with a fresh 500-cc. portion of benzene to dissolve any remaining pinacol. The original filtrate and the second portion of benzene, after it is filtered from the magnesium hydroxide, are mixed and distilled to one-half the original volume in order to remove the acetone; the remaining benzene solution is treated with 300 cc. of water and cooled to 10–15°. The pinacol hydrate separates and after about thirty minutes it is collected on a suction filter and washed with benzene, or better, the mixture is centrifuged in a basket centrifuge. The pinacol hydrate air-dried at room temperature (Note 8), weighs 325–375 g. (43–50 per cent of the theoretical amount based on the magnesium used). The product melts at 46–47°. It is sufficiently pure for most purposes. Occasionally the product is slightly yellow. If such a product is dissolved in an equal weight of boiling water, treated with a little bone-black, filtered, and the filtrate cooled in ice, over 95 per cent of the material may be recovered in large white crystals.

## 2. Notes

1. The condenser should have an inner tube with a fairly large diameter (12–15 mm.) in order to take care of the acetone vapors during the vigorous reaction.

2. The reaction mixture must be guarded carefully from moisture throughout the reaction; if moisture is present the magnesium becomes coated with oxide or hydroxide and the reaction does not take place smoothly.

3. If a larger amount of benzene is used, the reaction is too slow in starting. Commercial benzene is satisfactory if it has been distilled and the first portion containing the water rejected.

4. The acetone used is the ordinary commercial grade dried over calcium chloride. The dryness of the acetone is important and determines the time required for the reaction to start; if perfectly dry (two to three days over calcium chloride with occasional agitation) the reaction starts at once.

5. The reaction should be allowed to proceed with the maximum speed without losing acetone through the condenser. If the reaction is made to run slowly, the yields are lower.

6. It is important that the second portion of acetone and benzene be added to the reaction mixture before the refluxing stops, as otherwise heat must be applied to start the reaction again.

7. Mechanical stirring is rendered somewhat difficult in the laboratory because the mass becomes almost solid at the end of the reaction. A centrifugal tube type stirrer (Org. Syn. **3**, 29) may be used and will give satisfactory results.

8. If dried at a temperature above that of the room, there is a tendency for the product to melt and for pinacol to be lost by volatilization.

### 3. Other Methods of Preparation

The only practical method for the preparation of pinacol hydrate is the reduction of acetone and the procedure described above is a modification of that of Holleman.[1] The more common reducing agents that have been used are magnesium amalgam,[2] aluminum amalgam,[3] sodium,[4] and sodium amalgam.[5] Electrolytic reduction has also been used.[6]

[1] Rec. trav. chim. **25**, 206 (1906).

[2] Compt. rend. **140**, 721 (1905); Bull. soc. chim. (3) **33**, 454 (1905); (4) **7**, 454 (1910); Rec. trav. chim. **25**, 206 (1906); Ger. Pat. 233,894; Frdl. **10**, 1000 (1911); Eng. Pat. 411; C. A. **5**, 3152 (1911); U. S. Pat. 1,039,739; 1,039,740; C. A. **6**, 3495 (1912); French Pat. 459,313; C. A. **8**, 2780 (1914).

[3] Ger. Pat. 241,896; Frdl. **10**, 1000 (1911); U. S. Pat. 1,068,777; C. A. **7**, 3195 (1913); French Pat. 459,313; C. A. **8**, 2780 (1914); Ital. Pat. 135,560; C. A. **9**, 2797 (1915).

[4] Ann. **110**, 27 (1859); **111**, 279 (1859); **114**, 54 (1860); Jahresb. **1873**, 340; Ber. **27**, 455 (1894); Ger. Pat. 248,252; Frdl. **10**, 999 (1912).

[5] Ann. **124**, 327 (1862); Ann. Suppl. **3**, 375, footnote (1865).

[6] Ger. Pat. 113,719; Frdl. **6**, 22 (1900); Ger. Pat. 252,759; Frdl. **11**, 539 (1912).

XXX

## PINACOLONE

(Pinacoline)

$$(CH_3)_2C(OH)C(OH)(CH_3)_2 \rightarrow (CH_3)_3CCOCH_3 + H_2O$$

Submitted by C. A. HILL and E. W. FLOSDORF.
Checked by C. S. MARVEL and A. E. GRAY.

### 1. Procedure

IN a 2-l. round-bottom flask, fitted with a stopper carrying a dropping funnel and a connection to a condenser set for distillation, are placed 750 g. of 6 N sulfuric acid (Note 1) and 250 g. of pinacol hydrate (Note 2). The mixture is then distilled until the upper layer of distillate ceases to increase in volume (Note 3). This requires about fifteen to twenty minutes. The pinacolone layer in the distillate is separated from the water and the water is returned to the reaction flask. First, 60 cc. of concentrated sulfuric acid is added to the water, and then a second 250-g. portion of pinacol hydrate. The distillation is repeated. This process is repeated twice more until 1 kg. of pinacol hydrate has been used (Note 4).

The combined pinacolone fraction is dried over calcium chloride, filtered, and fractionally distilled. There is first a small low-boiling portion; then the pinacolone comes over at 103–107°; and finally there is a higher-boiling portion which yields more pinacolone on redistillation. The yield from a run, as described, is 287–318 g. (65–72 per cent of the theoretical amount). This product occasionally turns slightly yellow on standing, but redistillation removes the color with almost no loss of product.

## 2. Notes

1. Phosphoric acid (50 per cent) or hydrated oxalic acid may be used to bring about this rearrangement. When these reagents are used, the reaction mixture should be boiled for three to four hours. A yield of pinacolone corresponding to 60–65 per cent of the theoretical amount is thus obtained.

2. The pinacol hydrate is the unrecrystallized product obtained as described on page 87. The use of recrystallized pinacol hydrate increases the yield of pinacolone about 4 per cent.

3. An oily layer always remains behind in the distilling flask.

4. Larger or smaller runs of pinacolone may be made without materially affecting the yield.

## 3. Other Methods of Preparation

Pinacolone has been prepared by heating pinacol hydrate with dilute sulfuric acid or dilute hydrochloric acid;[1] by treating anhydrous pinacol[2] with concentrated sulfuric acid at 0°; by heating pinacol with 5 per cent oxalic acid[3] for twelve hours, or with 50 per cent tartaric, phosphoric, or oxalic acid[3] for three to four hours.

[1] Ann. **114**, 56 (1860); Bull. soc. chim. (4) **7**, 459 (1910); J. Am. Chem. Soc. **45**, 1559 (1923).

[2] Ber. **28**, 1364, footnote (1895); Chem. Zentr. **1906, II,** 496.

[3] Ber. **30**, 2266 (1897); Bull soc. chim. (4) **7**, 459 (1910).

# SEMICARBAZIDE SULFATE

$$NH_2CONHNO_2 + H_2SO_4 + 6H \text{ (electrolytic)} \rightarrow NH_2CONHNH_2 \cdot H_2SO_4 + 2H_2O$$

Submitted by A. W. Ingersoll, L. J. Bircher, and M. M. Brubaker.
Checked by Henry Gilman and L. C. Heckert.

## 1. Procedure

A. *Apparatus:*

The reduction is carried out in a 6×9 inch battery jar (Note 1), which is surrounded by a vessel suitable for a cooling bath. The bottom of the battery jar is covered with mercury, which serves as the cathode of the cell. The anode is a heavy lead coil separated from the catholyte by being suspended in a porous cup. This cup sets upon a support which holds it just above the cathode surface and does not appreciably diminish the latter (Note 2). The cathode is connected with the circuit by means of a glass tube partially filled with mercury and carrying a small piece of platinum wire sealed through the lower end. An efficient mechanical stirrer is provided in the catholyte. The current used in these experiments was 110 D.C., with a field rheostat, having a resistance of 8 ohms and a capacity of 20 amperes, for controlling the current. Any source of current supplying 30–110 volts and 15–20 amperes and any rheostat capable of carrying this current may be used. An ammeter reading to at least 15 amperes is connected in the circuit. Several reduction cells of the size described above may be run at one time, if they are connected in series. Fig. 3 shows the general set-up.

B. *Reduction of Nitrourea:*

After the apparatus is assembled, 600 cc. of 20 per cent sulfuric acid (Note 3) is placed in the battery jar, and the lead anode in the porous cup is also covered with acid of the same strength. The cell is surrounded by an ice-salt bath, the stirrer is started, and, while the solution is cooling, 50 g. of nitrourea (Note 4) is added to the catholyte. A thermometer is placed in the catholyte, and when the temperature drops to $+5°$ the current is turned on as follows: with the rheostat set for maximum resistance, the current is switched on, then the rheostat is gradu-

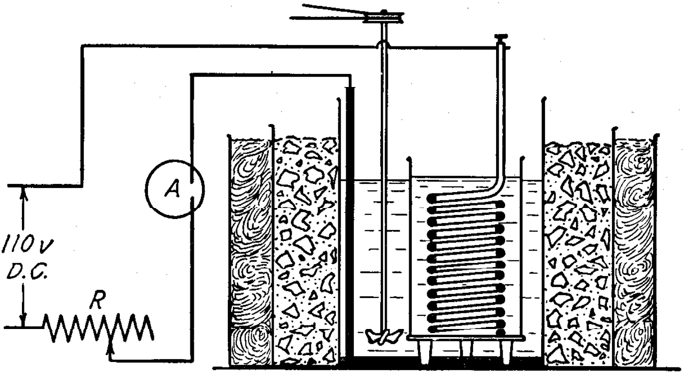



*Fig. 3.*

ally adjusted until the current flowing through the cell is about 0.06 amperes per square centimeter of cathode surface (Note 5). The cell must be efficiently cooled with ice and salt so as to keep the temperature at all times below 10° (Note 6). The reduction requires five to six hours. The nitrourea is quite insoluble, but gradually dissolves as it is reduced. The foam and clumps of solid are worked down into the liquid occasionally. When almost all the nitrourea is in solution, some of the catholyte should be drawn up with a pipette and used to wash down the nitrourea that adheres to the walls of the vessel. The reduction is continued for about ten to twenty minutes after the nitrourea has

dissolved. When the reduction is complete, as is indicated by a marked evolution of hydrogen, the current is shut off, and the porous cup is washed down with a little distilled water and removed. The solution of semicarbazide sulfate is removed from the cell and filtered (Note 7). The filtered solution is concentrated under reduced pressure on a water bath (Note 8) to a volume of 125–150 cc. Meanwhile, considerable semicarbazide sulfate will have crystallized. The mixture is cooled thoroughly in ice and the crystals are collected on a hardened filter paper, or better, on a filtros plate (see Note 5, p. 7), and washed several times with absolute alcohol to remove sulfuric acid. The crystals are dried on clay plate or paper. The yield is 50–57 g. (61–69 per cent of the theoretical amount) of a product melting at 144–145° with decomposition.

## 2. Notes

1. This is a commercial size. The internal diameter of these battery jars is 15–17 cm. Any sturdy glass vessel of the same dimensions may be used.

2. The lead anode should have about the same surface area as the cathode. In these experiments the porous cup used was 8 by 21 cm., but slightly larger sizes would do. A three-legged desiccator plate makes a convenient support for the cup. The latter should be immersed as deeply as possible in the catholyte, to decrease the resistance and consequent heating in the cell. It should not be more than 4–5 mm. thick, or the resistance will be too great and excessive heating will occur. Another convenient arrangement for the reduction cell is to divide the battery jar into two compartments by sealing in a diaphragm of thin corkpine wood by means of paraffin. This offers very little resistance to the passage of the current and allows the reduction to be carried on very rapidly. A filtros plate may also be used as a diaphragm to separate the two solutions.

3. For runs of this size, sulfuric acid as dilute as 15 per cent may be used with good results. In larger runs or in runs using moist nitrourea, the 20 per cent acid is preferable.

4. Various grades of nitrourea (p. 85) may be used in the reduction without noticeably affecting the purity of the semicarbazide sulfate. In order to obtain the yields given in the procedure, the nitrourea was well washed, sucked dry on the filter, and air-dried. The moist material obtained after filtration is equally good (see Note 3). Runs in which 60–70 g. of nitrourea was used gave slightly lower yields than when 50 g. was used.

5. The current varies somewhat with changes in temperature and concentration and must be adjusted occasionally. If very efficient cooling can be had, currents as high as 0.07 ampere per square centimeter may be used. The current efficiency and speed of reduction are decreased with currents below 0.06 ampere per square centimeter. A current of 13.5 amperes was satisfactory for the cell described.

6. The yield falls off rapidly at temperatures above 10°. The control of temperature is much easier if the porous cup is immersed as deeply as possible in the catholyte (Note 2).

7. If another run is to be made immediately, the reduced liquor may be removed by means of a siphon or pipette. If it is decanted, a little vaseline rubbed on the edge of the vessel will aid in pouring off the aqueous liquor from the mercury.

8. The evaporation must be conducted on a water bath whose temperature does not exceed 50–55°, in order to avoid decomposition of the product. The evaporation may also be conveniently carried out by placing the solution in a beaker, warming to 50–55°, and blowing air over the surface of the solution. This takes a somewhat longer time but requires no watching.

### 3. Other Methods of Preparation

Salts of semicarbazide have been prepared by the action of potassium cyanate on hydrazine sulfate;[1] by the action of hydrazine hydrate on urea;[2] by heating hydrazine ammonium carbonate;[3] by the reduction of nitrourea with zinc dust and hydro-

[1] Ber. **27**, 31 (1894).
[2] Ber. **27**, 56 (1894).
[3] Ber. **44**, 3485 (1911).

chloric acid;[4] by electrolytic reduction with iron cathodes and ammonium chloride solution,[5] with tin cathodes and sulfuric acid solution,[6] with lead cathodes and hydrochloric acid solution,[7] with cathodes of copper, nickel, lead and mercury in hydrochloric or sulfuric acid solution.[8] The present procedure has been devised from the last-mentioned research.

[4] Ann. **288**, 312 (1895).
[5] J. Chem. Soc. **79**, 1326 (1901).
[6] Rec. trav. chim. **31**, 25 (1912).
[7] Jap. Pat. 39,219; J. Chem. Soc. **122**, (1) 723 (1922).
[8] J. Am. Chem. Soc. **47**, 393 (1925).

# XXXII

## 1,2,3-TRIBROMOPROPANE

$$CH_2BrCH{=}CH_2 + Br_2 \rightarrow CH_2BrCHBrCH_2Br$$

Submitted by JOHN R. JOHNSON and W. L. MCEWEN.
Checked by ROGER ADAMS and L. T. SANDBORN.

### 1. Procedure

A 1-l. round-bottom flask is provided with a mechanical stirrer, a dropping funnel, a calcium chloride exit tube, and a thermometer which reaches nearly to the bottom of the flask. In the flask are placed 181.5 g. (1.5 moles) of allyl bromide (Note 1) and 250 cc. of dry carbon tetrachloride (Note 2). In the dropping funnel is placed 80 cc. (1.56 moles) of bromine which has been washed once with an equal volume of concentrated sulfuric acid. The mechanical agitation is started and the flask is cooled in a mixture of ice and salt. When the temperature has fallen to $-5°$, the bromine is allowed to drop in slowly at such a rate that the temperature remains at about $-5°$ and never rises above $0°$ (Note 3). The addition of the bromine requires about one and one-half hours. The solution is usually orange-red in color at the end of the reaction, owing to the slight excess of bromine. It is allowed to warm up to room temperature with continuous stirring (about one-half hour) and is then transferred to a large separatory funnel. The flask is washed once with a 10–15 cc. portion of carbon tetrachloride.

A 500-cc. Claisen flask is arranged for distilling the solvent and the solution is dropped in from the funnel at such a rate that the flask is never more than two-thirds full. The Claisen flask is heated in an oil bath, and the carbon tetrachloride distils when the oil bath reaches about 120°. As much as possible of

the solvent is removed at atmospheric pressure by allowing the temperature of the oil bath to rise to 150°. The remainder of the carbon tetrachloride is removed under a pressure of about 20 mm. by collecting a fraction until the thermometer registers a sudden rise (temperature of the oil bath about 120°).

The residue in the distilling flask is practically pure 1,2,3-tribromopropane (Note 4) and boils at 100–103°/18 mm. On cooling in an ice-salt mixture and scratching vigorously, the tribromopropane solidifies to a mass of white needles, which melt below room temperature. The yield is 406–413 g. (96–98 per cent of the theoretical amount). If an absolutely colorless product is desired, it is advisable to collect the first few drops of distillate separately, since they may be slightly yellow. The product on long standing becomes yellow, but when the colored product is used in reactions it gives yields that indicate a high degree of purity.

## 2. Notes

1. Allyl bromide (Org. Syn. 1, 3) was dried with calcium chloride and distilled through a fractionating column. The portion boiling from 69.5–71.5° was collected.

2. Carbon tetrachloride was purified by distilling the commercial product and rejecting the first 10 per cent of the distillate, thus eliminating the water.

3. A yield of 93 per cent of the theoretical amount is obtained when the reaction is run at a temperature of 25–30°. At the higher temperature, there is a small amount of high-boiling product left in the flask after the final distillation.

4. The crude 1,2,3-tribromopropane which remains after complete removal of the carbon tetrachloride weighs 418–420 g. It is almost pure and can be used for a number of reactions without further purification.

## 3. Other Methods of Preparation

Symmetrical tribromopropane (glycerol tribromohydrin) has been prepared by the action of phosphorus pentabromide on

either epibromohydrin [1] or symmetrical dibromohydrin,[1,2] and by the addition of bromine to allyl bromide [3] or iodide.[4] It has also been obtained by heating glyceryl triacetate with hydrogen bromide dissolved in glacial acetic acid.[3a] 1,2,3-Tribromopropane is also formed by the action of bromine, usually in the presence of iron wire or aluminium bromide, upon *n*-propyl,[5] isopropyl,[6] trimethylene,[5] or propylene [5,7] bromides.

The method described in the procedure is essentially that of Perkin and Simonsen.[3a]

[1] Ann. **101,** 76 (1857).
[2] Ann. **154,** 369 (1870).
[3] Ann. **156,** 168 (1870); (a) J. Chem. Soc. **87,** 859 (1905).
[4] Ann. **104,** 247 (1857).
[5] Ber. **24,** 4245 (1891).
[6] Ann. **136,** 63 (1865).
[7] Compt. rend. **127,** 274 (1898).

# XXXIII

## TRIMETHYLENE CYANIDE

$$BrCH_2CH_2CH_2Br + 2NaCN \rightarrow CNCH_2CH_2CH_2CN + 2NaBr$$

Submitted by C. S. MARVEL and E. M. McCOLM.
Checked by H. T. CLARKE and E. E. DREGER.

### 1. Procedure

IN a 5-l. round-bottom flask fitted with a stopper holding a reflux condenser and a separatory funnel, are placed 294 g. (6 moles) of sodium cyanide and 300 cc. of water. The flask is heated on a steam bath until most of the sodium cyanide is in solution. This requires two to three hours. A solution of 500 g. (2.47 moles) of trimethylene bromide (Note 1) in 1 l. of 95 per cent alcohol is then added through the separatory funnel over a period of forty to sixty minutes. The mixture is refluxed for thirty to forty hours (Note 2) on a steam bath. Then the solvent is removed, preferably under reduced pressure. The residue, consisting of sodium bromide, sodium cyanide, and trimethylene cyanide, is extracted with 300–400 cc. of ethyl acetate, which dissolves the trimethylene cyanide and does not dissolve the inorganic salts. This solution is filtered and the salt washed once with about 100 cc. of ethyl acetate. The ethyl acetate is distilled at ordinary pressure (Note 3) and the residual liquid is distilled under reduced pressure. The yield of trimethylene cyanide boiling at 144–147°/13 mm. or 131–134°/10 mm. is 180–200 g. (77–86 per cent of the theoretical amount).

### 2. Notes

1. Larger runs seem to give slightly lower yields.

2. The yield is lower if the heating is continued too long, owing to partial hydrolysis of the cyanide.

3. Very little ethyl acetate is lost in this procedure if it is distilled at ordinary pressures. If it is not entirely removed before the pressure is reduced, considerable foaming occurs.

## 3. Other Methods of Preparation

The only practical method of preparation for trimethylene cyanide is the action of potassium cyanide on trimethylene bromide.[1]

[1] Compt. rend. **82**, 1197 (1876); **100**, 742 (1885); Bull. soc. chim. (2) **43**, 617 (1885); J. Chem. Soc. **55**, 702 (1889).

# INDEX

# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

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# PREFACE TO VOLUME VI

THE general plan of this series as set forth in preceding volumes has been followed in the present volume. It is a great pleasure to acknowledge the cordial response of former and new contributors, particularly those in other countries. In this volume twenty-seven of the thirty preparations have been submitted by twenty-three contributors, ten of whom are of foreign countries.

In continuance of the policy of including improved directions for preparations published in previous volumes, a new set of directions is given for the preparation of benzil.

Several new features are inaugurated in the present volume. To the cumulative subject index to the six volumes which have already appeared, a similar author index is now added. In order to bring literature references to methods of preparative value up to date, there has been included an appendix which contains later references to directions published previously in this series. The appendix also contains corrections to some of the earlier preparations. The editors acknowledge their appreciation of the assistance rendered by those who submitted corrections and suggestions, and welcome heartily any comments calculated to improve the series.

The editors regret that pressure of other work has made it impossible for Dr. Oliver Kamm to continue his valuable services with this series.

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# ORGANIC SYNTHESES

## I

## ACROLEIN

$$CH_2OHCHOHCH_2OH \rightarrow CH_2{=}CHCHO + H_2O$$

Submitted by HOMER ADKINS and W. H. HARTUNG.
Checked by FRANK C. WHITMORE and M. L. WOLFROM.

### 1. Procedure

THE apparatus is assembled according to Fig. 1. *B* and *D* are 5-l. round-bottom flasks, immersed to about two-thirds of

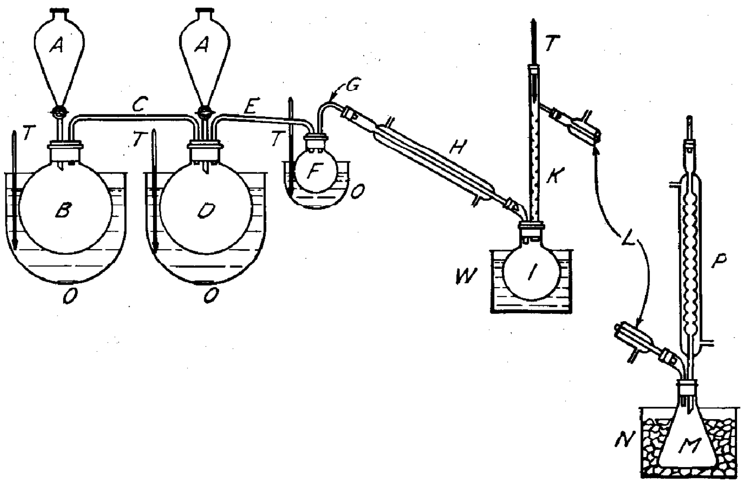



FIG. 1.

their height in deep oil baths heated by large burners. Each bath is provided with a thermometer reaching to the level of the bottom of the flask. Flask *B* is fitted with a specially treated

two-hole cork stopper (Note 1), in one hole of which is fitted a 500-cc. separatory funnel *A* and in the other a delivery tube *C* of 12-mm. diameter. The tubes must not extend more than 3 mm. below the stopper. Flask *D* is fitted with a three-hole cork stopper connected with a separatory funnel, the delivery tube from *B*, and the delivery tube *E* of 12-mm. tubing leading to flask *F*. *F* is a 500-cc. round-bottom flask immersed to two-thirds of its height in an oil bath heated by a Bunsen burner and provided with a thermometer.

Flask *F* is provided with a two-hole cork stopper connected with tube *E*, and with tube *G* which connects with the first condenser *H* and may be of smaller bore than tubes *C* and *E*. *H* is a condenser with a 30-cm. water jacket. *H* is connected with *I* by means of an adapter. *I* is a 1-l. round bottom flask supported in a pan which is at first filled with ice and later used as a water bath. Flask *I* is fitted with a two-hole cork stopper carrying the adapter connected with condenser *H* and a Vigreux column *K* of 2-cm. diameter and a length of 30 cm. to the side arm. Flask *I* and condenser *H* are covered with black cloth (Note 2). The side arm of *K* is connected with a 90-cm. water-jacketed condenser *L* which leads into *M* through an adapter. *M* is a 750-cc. Erlenmeyer flask immersed in an ice bath. Flask *M* is provided with a two-hole stopper connected with the adapter from *L* and an upright bulb condenser that is provided with a tube leading through a window or to a hood.

Before the final assembling of the apparatus, the flasks are charged as follows: One kilo of freshly fused and finely powdered acid potassium sulfate, 200 g. of powdered potassium sulfate, and 300 g. of dry glycerol (Note 3) are thoroughly mixed in each of flasks *B* and *D*. In each of flasks *I* and *M* is placed about 1 g. of hydroquinone to act as a stabilizer for the acrolein (Moureu, *Compt. rend.*, **170**, 26 (1920)).

The apparatus is assembled as indicated and the oil baths under *B* and *D* are heated to about 190–200° (Note 4), and the oil bath under *F* to about 110–120°. The bath under *I* is filled with ice. The volatile products are collected in *I* which is kept carefully protected from light. After the first violent reaction has

abated (about one hour) the baths under *B* and *D* are raised to 215–230° and maintained there until no more volatile product comes over (a total time of heating of about four and one-half hours). When the reaction is well started 300 g. of dry glycerol is placed in each separatory funnel, and added drop by drop during the heating. After *B* and *D* have been heated about four hours the ice under *I* is replaced by water which is heated to 75–80° to distil the acrolein into flask *M*, which is packed in ice. Near the end of the distillation the water under *I* is heated to boiling.

The product in *M* is treated with small amounts of solid sodium bicarbonate to neutralize any acid present. The cold liquid is filtered through a small filter into a 1500-cc. distilling flask containing about 1 g. of hydroquinone. It is then distilled into a tared dark bottle containing about 1 g. of hydroquinone. The yield of product boiling at 52.5–55.5° (Note 5) obtained from 1200 g. (13 moles) of dry glycerol is 240–350 g. (33–48 per cent of the theoretical amount).

## 2. Notes

1. The corks used in the apparatus are made tight and heat-resistant by treatment with sodium silicate solution. After being properly fitted and bored they are placed in the silicate solution contained in a bottle that is connected with a suction pump. The solution is forced into the pores of the corks by alternately making and breaking the vacuum and shaking the solution vigorously. After the excess of solution has been wiped off, the corks are put in place while still wet. After this the outside of each cork is given an extra coat of the silicate solution. When corks treated in this way were used no odor of acrolein was noted in the laboratory.

2. The exclusion of light slows up the polymerization of the acrolein. If the condensers are not protected from light a solid polymer collects in them.

3. The glycerol is dehydrated by heating slowly in an an open dish in a hood until the temperature of the liquid is 170°. A

sand bath is used and the heating requires about three hours. "Dynamite glycerine," 96–98 per cent, may be used instead of the dried glycerol.

4. The heating must not be too rapid nor too high at first as there is danger of frothing followed by a clogging of the apparatus.

5. Pure acrolein boils at 52.5°/760 mm. (Moureu, Boutaric and Dufraisse, *J. chim. phys.* **18**, 333 (1921)).

## 3. Other Methods of Preparation

Satisfactory methods for the preparation of acrolein have been described by Wohl and Mylo,[1] Witzemann,[2] and Moureu.[3] In the Wohl and Mylo method the vapors of glycerol are passed over magnesium sulfate maintained at 330–340.° Witzemann's method involves the use of magnesium sulfate at elevated temperatures with the consequent danger of breaking the generating flasks. Moureu's method involves apparatus not always available.

[1] Ber. **45**, 2046 (1912).

[2] J. Am. Chem. Soc. **36**, 1766 (1914).

[3] Compt. rend. **169**, 805 (1919). Ann. chim. (9), **15**, 176 (1921).

II

# BENZIL

$$C_6H_5CHOHCOC_6H_5 + (O) \rightarrow C_6H_5COCOC_6H_5 + H_2O$$

Submitted by H. T. CLARKE and E. E. DREGER.
Checked by ROGER ADAMS and GERALD H. COLEMAN.

## 1. Procedure

IN a 12-l. flask, fitted with a mechanical stirrer and mercury seal, reflux condenser and an inlet tube for the introduction of air, is placed a mixture of 4100 g. (16.4 moles) (Note 1) of crystalline copper sulfate (Note 2), 4000 g. of technical pyridine and 1600 g. of water. This is heated on a steam bath with stirring until the copper sulfate is completely dissolved and then 1696 g. (8 moles) of benzoin (Org. Syn. **1**, 33; uncrystallized material is satisfactory) is added and heating and stirring continued for two hours. The reaction mixture becomes dark green in color and the melted benzil forms the upper layer. After cooling, the copper sulfate-pyridine solution is decanted and the benzil washed with water and then heated with 3–4 l. of 10 per cent hydrochloric acid. After cooling, the benzil is filtered, washed with water, dried and recrystallized from carbon tetrachloride (2 l. of solvent per kg. of benzil). By concentration of the mother liquors a certain amount of benzil is always obtained. The total yield is 1450 g. (86 per cent of the theoretical amount) of recrystallized material melting at 94–95° (Note 3).

The copper sulfate-pyridine mixture is readily reoxidized by passing a current of air through it for thirty-six hours (Note 4). To this resulting solution is now added 200 g. of pyridine and it is then used for oxidizing another batch of 1696 g. of benzoin.

## 2. Notes

1. In checking this preparation, runs about 25 per cent of the size described were made. The yields were about 3 per cent less

than in the larger runs. For the reoxidization of the smaller amount of copper sulfate-pyridine solution, air was passed through for fifteen hours.

2. Copper hydroxide (or carbonate) does not dissolve in pyridine.

3. In comparing the copper sulfate-pyridine method with the nitric acid method (Org. Syn. **1**, 25) it should be pointed out that the constants on the samples are as follows:

| Method | m. p. crude | m. p. recryst. | Fehling's Test on recryst. |
|---|---|---|---|
| Copper sulfate-pyridine | 94–95° | 94–95° | Negative |
| Nitric acid | 88° | 93–94° | Positive |

In other words, by the nitric acid oxidation it is difficult to obtain a product completely free from benzoin. The yields by the nitric acid method are generally about 95–96 per cent, whereas with the copper sulfate-pyridine method the yield drops to approximately 86 per cent.

4. Fifteen hours was found not long enough to effect a complete oxidation.

### 3. Other Methods of Preparation

These are discussed in Org. Syn. **1**, 26. The foregoing method is based on the observation of E. Fischer[1] that benzoin reduces Fehling's solution in the cold. Pyridine was selected as it prevents the precipitation of cuprous oxide, is not so volatile as ammonia, and acts as a partial solvent for the benzoin.

Mohler[2] has just shown that copper, pyridine and air oxidize benzoin to benzoic acid. Also, the same oxidation takes place in the absence of copper.

The melting temperatures of mixtures of benzil and benzoin have been recorded by Vanstone,[3] who showed that the maximum possible depression is about 10°.

[1] Ann. **211**, 214 (footnote) (1882).

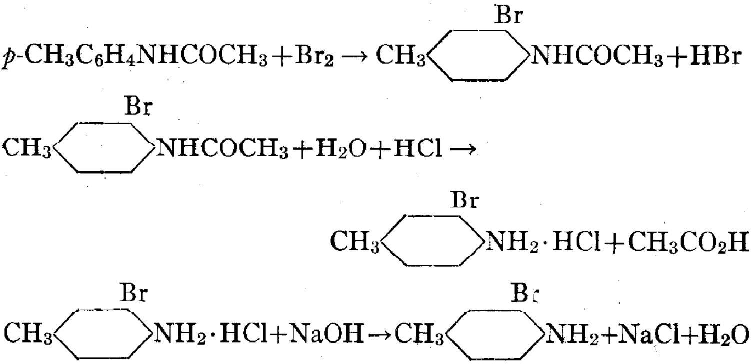
[2] Helvetica Chim. Acta, 8, 740 (1925).

[3] J. Chem. Soc. **95**, 600 (1909).

III

## 3-BROMO-4-AMINOTOLUENE

$$p\text{-}CH_3C_6H_4NH_2 + CH_3CO_2H \rightarrow p\text{-}CH_3C_6H_4NHCOCH_3 + H_2O$$



Submitted by J. R. JOHNSON and L. T. SANDBORN.
Checked by FRANK C. WHITMORE and A. M. GRISWOLD.

### 1. Procedure

*p*-Acetotoluide is prepared by refluxing 214 g. (2 moles) of commercial *p*-toluidine with 800 cc. of glacial acetic acid in a 2-l. round-bottom flask for two hours. The reflux condenser is replaced by a mechanical stirrer and the mixture is stirred and cooled to 45°. Part of the product may separate in small crystalline flakes. The mixture is thoroughly stirred and 325 g. (2.03 moles) of bromine (106 cc.) is added slowly from a separatory funnel at such a rate that the temperature of the mixture is maintained at 50–55°. During the course of this addition, which requires about forty minutes, a precipitate may separate; this later dissolves. The mixture is stirred half an hour after the

bromine has been added, and is then poured in a thin stream (Note 1) with efficient stirring into 10 l. of cold water to which has been added 25 g. of sodium bisulfite (Note 2).

The 3-bromo-4-acetaminotoluene separates in crystalline flocks. It is filtered by suction and washed well with water and pressed dry. The wet crude material is dried until its weight does not exceed 500 g. before proceeding with the hydrolysis (Note 3).

The partially dried 3-bromo-4-acetaminotoluene is refluxed with 500 cc. of 95 per cent ethyl alcohol in a 3-l. round-bottom flask. To the boiling solution is added 500 cc. of concentrated hydrochloric acid and the refluxing is continued for three hours. During this time, crystals of the hydrochloride of 3-bromo-4-aminotoluene separate. The hot mixture is poured into a 2-l. beaker and cooled thoroughly in running water. The hydrochloride is filtered by suction and washed rapidly with two 100-cc. portions of chilled alcohol. The weight of the hydrochloride is 250–300 g. (Note 4).

The hydrochloride is suspended in 800 cc. of water in a 2-l. beaker provided with a mechanical stirrer. The base is liberated by the addition of a solution of 140 g. of technical sodium hydroxide in 700 cc. of water, and settles as a heavy brownish oil. After cooling to room temperature, the oil is separated and weighed. The yield of the crude base is 225–250 g. (60–67 per cent of the theoretical amount based on the amount of toluidine used). The crude material may be used directly for the preparation of *m*-bromotoluene (p. 16).

The base may be purified by steam distillation but distillation under reduced pressure is more satisfactory. The oil is dried over 5 g. of solid sodium hydroxide and distilled in vacuo. The first portion of the distillate may contain *p*-toluidine and must be carefully separated, as it causes rapid discoloration. The 3-bromo-4-aminotoluene is obtained as a colorless liquid of b.p. 120–122°/30 mm. or 92–94°/3 mm. It solidifies on cooling and melts at 16–18°. The loss on purification is about 15 per cent of the weight of the crude base.

## 2. Notes

1. The first of the bromine compound often separates as a heavy oil. To avoid the formation of lumps, this material should be seeded or allowed to crystallize spontaneously before the main portion is poured into water.

2. If the color of bromine persists, more sodium bisulfite should be added.

3. If the material is not partly dried before hydrolysis, the yield of the hydrochloride is diminished because of its solubility. If pure 3-bromo-4-acetaminotoluene is desired, the crude material may be crystallized from 50 per cent alcohol with the addition of decolorizing carbon (Norite) as almost colorless needles, m.p. 116–117°. The yield is 360 g. (79 per cent of the theoretical amount). This purification has no advantage when the acetamino compound is to be hydrolyzed to the amine.

4. The dark filtrate from the hydrochloride does not contain enough dissolved salt to justify recovery unless the acetamino compound was insufficiently dried before the hydrolysis.

## 3. Other Methods of Preparation

The bromination of *p*-acetotoluide, followed by hydrolysis of the resulting bromoacetotoluide[1] is the only practical method which has been used for making 3-bromo-4-aminotoluene. The present process is a modification of the method described by Feitler.[2]

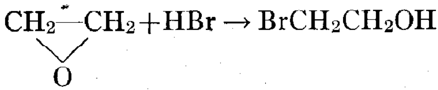
[1] Ann. **168**, 153 (1873).

[2] Z. physik. Chem. **4**, 77 (1889).

# IV

## 2-BROMOETHANOL

(Ethylene Bromohydrin)



Submitted by F. K. THAYER, C. S. MARVEL and G. S. HIERS.
Checked by HENRY GILMAN and F. SCHULZE.

### 1. Procedure

IN the 1-l. three-necked flask *A* (**Fig.** 2) is placed 550 cc. (4.25 moles) of 46 per cent hydrobromic acid (sp. g. 1.46) (Note 1). Ethylene oxide (Note 2) is led into the acid solution as indicated in the diagram. The tank *E* is arranged on a balance so that the amount of ethylene oxide which is used can be weighed. *B* is a U-tube containing water to indicate the rate of flow of the gas. *D* is a glass coil surrounded by ice and salt which cools the gas nearly to the liquefaction temperature. *C* is another U-tube containing water which shows whether or not the gas is being completely absorbed.

The flask *A* is surrounded by an ice-salt bath and the stirrer is started. When the temperature of the acid has dropped to 10°, 132 g. (3 moles) of ethylene oxide is added over a period of about two and one-half hours (Note 3). The stirring is continued for one hour (Note 4) after all of the ethylene oxide has been added and the temperature is maintained below 10° during the reaction.

After this time the excess hydrobromic acid is neutralized with excess sodium carbonate, of which about 100 g. of anhydrous salt is required. To the aqueous solution is then added about 100 g. of anhydrous sodium sulfate until some of the solid does

not dissolve. A layer of ethylene bromohydrin separates and is collected in 200 cc. of ether. The ether layer is below the aqueous layer. The solid sodium sulfate is filtered from the solution and washed once or twice with a small amount of ether (Note 5) to remove any mechanically held bromohydrin. The aqueous filtrate is twice extracted with 200-cc. portions of ether (Note 6). The combined ether extracts are dried over night with anhydrous sodium sulfate, filtered and distilled from a steam bath (Note 7). The remaining bromohydrin is distilled under reduced pressure

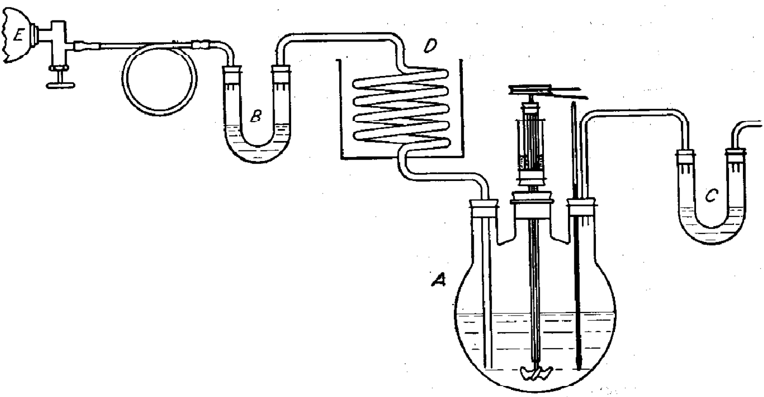



FIG. 2.

(Note 8). After two distillations the fraction boiling at 55–59°/22 mm. (Note 9) is pure ethylene bromohydrin. The yield is 327–345 g. (87–92 per cent of the theoretical amount).

## 2. Notes

1. An equivalent amount of hydrobromic acid of greater strength may be used. Acid of lower concentration gives a much lower yield. The preparation of 48 per cent hydrobromic acid is described in Org. Syn. 1, 2.

2. Ethylene oxide attacks rubber very rapidly. Hence if rubber is used to connect the glass tubes which conduct the gas to the reaction flask, care must be taken to have the glass tubes meet inside the rubber tubing.

3. The ethylene oxide must be added quite rapidly in order to complete the addition in the time specified. It should be added at a maximum possible rate consistent with practically no loss of ethylene oxide through tube *C*. The best absorption of ethylene oxide appears to take place when the temperature is kept between 0° and 10°. Absorption cannot be completed in two and one-half hours when the temperature is kept at 0°.

4. When the mixture is stirred too long or the temperature is allowed to rise much above 10° the yields are lower.

5. The ether used to wash the sodium sulfate crystals may be used for the extraction of the aqueous solution.

6. When the bromohydrin is removed by the first treatment with ether, the ethereal layer is on the bottom. Subsequent ethereal extractions float on the aqueous layer.

7. About 300–335 cc. (50–55 per cent) of ether is recovered.

8. A modified Claisen flask (Org. Syn. **1**, 40) was used to fractionate the compound. Distillation under atmospheric pressure causes some decomposition (Read and Williams, *J. Chem. Soc.* **117**, 1216 (1920)).

9. In the first distillation the fraction boiling at 50–65°/22 mm. is collected. Boiling points observed at other pressures are as follows: 47–51°/15 mm.; 59–63°/25 mm.; and 90–94°/80 mm.

### 3. Other Methods of Preparation

Ethylene bromohydrin has been prepared by the reaction between ethylene glycol and hydrobromic acid[1] and phosphorus tribromide.[2] It has also been prepared by the direct addition of hypobromous acid to ethylene,[3] and by the reaction between ethylene and dilute bromine water.[4] With ethylene oxide now available at a reasonable price, the method described is probably the best because of the high yields and the convenience of reaction.

[1] Jahresber. **1872**, 304; J. Am. Chem. Soc. **38**, 1079 (1916); Acad. Sci. Fennicae. **3A**, 1-103 (C. A. **1920**, 2176).

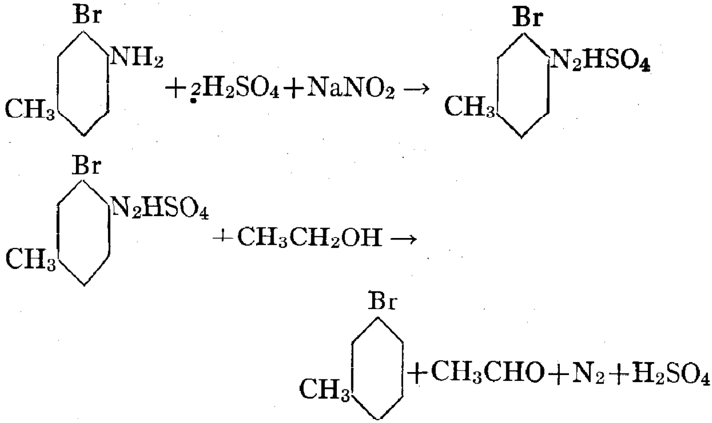
[2] Ber. **9**, 48 (1876).

[3] J. Russ. Phys. Chem. Soc. **30**, 900 (1898) (Chem. Zentr. **1899**, II, 591).

[4] J. Chem. Soc. **111**, 241 (1917); **117**, 1214 (1920); **129**, 409 (1926).

V

## m-BROMOTOLUENE



Submitted by L. A. BIGELOW, J. R. JOHNSON and L. T. SANDBORN.
Checked by FRANK C. WHITMORE and A. M. GRISWOLD.

### 1. Procedure

To a cold mixture of 800 cc. of 95 per cent ethyl alcohol and 200 cc. of concentrated sulfuric acid (Note 1) in a 5-l. round-bottom flask, provided with an efficient mechanical stirrer, is added 250 g. (1.33 moles) of crude 3-bromo-4-aminotoluene (p. 8). The solution is stirred and cooled to 10° and a solution of 148 g. (2.05 moles) of U.S.P. sodium nitrite in 260 cc. of water is added from a separatory funnel. During this addition, the temperature of the mixture must not be allowed to rise above 10°. After all of the nitrite solution has been added, the mixture is stirred twenty minutes longer to complete the diazotization.

To the diazotized solution is added 35 g. (0.55 mole) of copper bronze (Note 2) which has been washed with ether. The stirrer is replaced by a long, efficient reflux condenser. A bath of ice water is prepared for cooling the flask when the reaction becomes

too vigorous. The flask is warmed cautiously until a vigorous evolution of gas starts. It is then immersed in the ice water to prevent loss through the condenser by too rapid evolution of nitrogen and acetaldehyde. When the reaction has moderated, the flask is again warmed, and finally the mixture is heated for ten minutes on a steam bath. At the end of the reaction the color changes from reddish brown to yellow.

After the addition of 2 l. of water, the mixture is steam-distilled as long as any oil comes over. The crude, heavy, yellow oil is separated and washed with two 200-cc. portions of 10 per cent sodium hydroxide, once with 100 cc. of water, twice with 150-cc. portions of concentrated sulfuric acid, and finally with 100 cc. of 5 per cent. sodium carbonate solution. It is dried with about 5 g. of calcium chloride, filtered through glass wool, and distilled using a long air condenser. Most of the product boils at 180–183°/750 mm. The yield of pure colorless material, b.p. 183°/760 mm., is 125–135 g. (36–39 per cent of the theoretical amount, based on the amount of *p*-toluidine originally used, or 54–59 per cent based on the amount of 3-bromo-4-aminotoluene).

## 2. Notes

1. Proper care must be exercised in mixing the alcohol and sulfuric acid. The mixture is best cooled in the flask with stirring.

2. Reduced copper powder and various grades of copper bronze were used with practically the same results.

## 3. Other Methods of Preparation

*m*-Bromotoluene has been prepared by the diazotization of *m*-toluidine followed by treatment with cuprous bromide, potassium bromide and hydrobromic acid.[1] It has also been obtained by elimination of the amino group from 3-bromo-4-aminotoluene[2,3] and 5-bromo-2-aminotoluene.[4] The present process is a modification of the method of Feitler.[3]

[1] Ber. **37**, 994 (1904).
[2] Ann. **168**, 155, 158 (1873).
[3] Z. physik. Chem. **4**, 77 (1889).
[4] Ann. **168**, 164 (1873).

VI

# $p$-CHLOROPHENYL ISOTHIOCYANATE

$$p\text{-}ClC_6H_4NH_2 + CSCl_2 \rightarrow p\text{-}ClC_6H_4NCS + 2HCl$$

Submitted by G. MALCOLM DYSON.
Checked by FRANK C. WHITMORE and P. L. CRAMER.

## 1. Procedure

IN a 5-l. crock or battery jar, provided with a powerful mechanical stirrer, are placed 3.5 l. of water and 249 g. (2.16 moles) of thiophosgene (p. 86) (Note 1). To the vigorously stirred (Note 2) mixture is added slowly 255 g. (2 moles) of $p$-chloroaniline during about one-half hour. The stirring is continued for about an additional half-hour. The dark brown oil is separated, washed with 50 cc. of 10 per cent hydrochloric acid, and placed in a flask for steam distillation.

The flask is immersed in an oil bath heated to 120° and dry steam is then passed through the reaction mixture. The first few cubic centimeters of distillate contain the excess of thiophosgene and are discarded. The isothiocyanate passes over with the water as an oil that solidifies on cooling. The steam distillation requires about four hours. The crude material is crystallized from two parts of ethyl alcohol at 50°, from which it separates as white needles melting at 44–45°. The yield is 245–275 g. (72–81 per cent of the theoretical amount) (Note 3).

## 2. Notes

1. Because of the objectionable properties of thiophosgene, care should be exercised in its use.

2. The stirring at the start must be very vigorous or the yield is decreased.

3. The method is general for alkyl- and halogen-substituted aromatic amines.

## 3. Other Methods of Preparation

*p*-Chlorophenyl isothiocyanate has also been prepared by treating an alcoholic solution of *sym*-di-*p*-chlorophenyl thiourea with iodine,[1] from ammonium *p*-chlorophenyldithiocarbamate and lead nitrate,[2] (p. 72), and from the action of thiophosgene with *p*-chloroaniline.[3]

[1] Ber. **5**, 156 (1872).
[2] Univ. Kansas Sci. Bull. **13**, 1 (1922).
[3] J. Chem. Soc. **125**, 1702 (1924).

## 3-CYCLOHEXYL-2-BROMOPROPENE-1

$$C_6H_{11}MgBr + CH_2BrCBr{=}CH_2 \rightarrow C_6H_{11}CH_2CBr{=}CH_2 + MgBr_2$$

*Submitted by* R. LESPIEAU *and* M. BOURGUEL.
Checked by ROGER ADAMS and M. M. BRUBAKER.

### 1. Procedure

A 3-l. three-necked, round-bottom flask is fitted with a mechanical stirrer through a mercury seal, a reflux condenser and a 1-l. separatory funnel. A mixture of 200 g. (1 mole) of 2,3-dibromopropene (Org. Syn. **5**, 49) and 200 cc. of dry ether is added. The flask is now cooled in an ice bath, the stirrer is started, and one molecular equivalent of cyclohexylmagnesium bromide, prepared from 31 g. of magnesium, 204 g. of cyclohexyl bromide and 400 cc. of dry ether (Note 1) is added at such a rate that the mixture refluxes gently (Note 2). The addition takes about one-half to three-quarters of an hour. Two layers are formed and magnesium bromide may or may not separate.

The stirring should be continued and the ice bath replaced by a hot-water bath, and the mixture refluxed gently for two hours. The flask is again cooled and 30 cc. of concentrated hydrochloric acid in 350 cc. of water is added through the separatory funnel. This should be added slowly as long as heat is evolved. The contents of the flask are then transferred to a separatory funnel, the ether layer separated and dried over calcium chloride.

The ether is distilled on a steam bath (Note 3) and the residue fractionated under reduced pressure by means of a 20-cm. column (Org. Syn. **1**, 40). After three fractionations, there is obtained 32–44 g. of a product boiling up to 100°/25 mm., which is mainly unchanged dibromopropene (b.p. 42–43°/18 mm.), and

123–130 g. (60.5–64 per cent of the theoretical amount, not taking into account recovered dibromopropene) of cyclohexylbromopropéne (Note 4) boiling at 100–105°/25 mm. This material is satisfactory for most purposes. On redistillation it boils at 88–89°/14 mm.

## 2. Notes

1. The preparation of cyclohexylmagnesium bromide is described on p. 22. The solution may be standardized by titrating against 0.5 N hydrochloric acid, and exactly one mole equivalent is used in the preparation. Five cubic centimeters of cyclohexylmagnesium bromide solution is slowly added to 20 cc. of water, an excess of the standard acid is added, and the excess acid titrated with sodium hydroxide. If 85 g. (3.5 moles) of magnesium, one liter of dry ether, and 571 g. of cyclohexyl bromide (3.5 moles) are used, a solution results which is about 2 molar.

Excess of Grignard reagent may be employed and the same yield obtained, so that the titration is an aid to conserving Grignard reagent. About an 80 per cent yield of cyclohexylmagnesium bromide from cyclohexyl bromide and magnesium can generally be depended upon.

2. The reaction is instantaneous and is not stopped by moderate cooling. The cooling may be dispensed with and the cyclohexylmagnesium bromide added more slowly (two hours).

3. The ether solution may be added in several portions to a 500-cc. modified Claisen flask (Org. Syn. **1**, 40) and the ether distilled after each addition.

4. By a similar procedure benzylmagnesium chloride and 2,3-dibromopropene give 4-phenyl-2-bromobutene-1 in about 45 per cent yield, b.p. 119°/20 mm.; and heptylmagnesium bromide and 2,3-dibromopropene give 2-bromodecene-1 in 60–65 per cent yields, b.p. 76–77°/3 mm.

## 3. Other Methods of Preparation

3-Cyclohexyl-2-bromopropene-1 has been made by the action of cyclohexylmagnesium bromide on 2,3-dibromopropene.[1]

[1] Bull. soc. chim. (4) **29**, 528 (1921)

VIII

## CYCLOHEXYLCARBINOL

$$C_6H_{11}Br + Mg \rightarrow C_6H_{11}MgBr$$

$$C_6H_{11}MgBr + HCHO \rightarrow C_6H_{11}CH_2OMgBr$$

$$C_6H_{11}CH_2OMgBr + H_2O \rightarrow C_6H_{11}CH_2OH + Mg(OH)Br$$

Submitted by ROGER ADAMS and C. R. NOLLER.
Checked by HENRY GILMAN and J. E. KIRBY.

### 1. Procedure

IN a 1-l. three-necked, round-bottom flask fitted with a mechanical stirrer through a mercury seal, a separatory funnel and an efficient reflux condenser to which a calcium chloride tube is attached, are placed 25 g. (1.03 moles) of magnesium turnings, 140 cc. of dry ether, and a small crystal of iodine. The stirrer is started and a small portion (about 10 cc.) of a solution of 118.5 g. (1 mole) of cyclohexyl bromide (Note 1) in 120 cc. of dry ether is added through the separatory funnel. After the reaction starts, the remainder of the solution is run in at such a rate that the whole is added at the end of forty-five minutes. The mixture is stirred and refluxed for an additional thirty to forty-five minutes.

The separatory funnel is now replaced by a wide glass tube (about 12 mm. internal diameter) which passes well into the flask but does not dip below the surface of the liquid (Note 2). This tube connects directly with a 500-cc. round-bottom flask containing 50 g. of paraformaldehyde which has been previously dried for two days in a vacuum desiccator over phosphorus pentoxide. The stirrer is started (Note 3) and the flask containing the paraformaldehyde is heated in an oil bath to 180–200°,

when depolymerization takes place and gaseous formaldehyde (Notes 4 and 5) passes into the Grignard reagent. At the end of about two and one-half hours most of the paraformaldehyde has been depolymerized and the reaction is complete (Note 6).

The reaction mixture is then transferred to a 2-l. round-bottom flask with wide neck, and to this is added all at once 300 g. of cracked ice, and the mixture is rapidly agitated by a rotary motion until the decomposition is complete (Note 7). Sufficient 30 per cent sulfuric acid is added to dissolve the magnesium hydroxide, and the mixture is then steam-distilled until oil no longer collects on the surface of the distillate. The distillate, which amounts to 1500–2500 cc., is saturated with sodium chloride and the upper layer separated. The aqueous layer is extracted with two 100-cc. portions of ether and the ether extract added to the alcohol layer. The ether solution is dried over anhydrous potassium carbonate, filtered, and heated carefully on the steam cone until all the ether is distilled. The crude alcohol is warmed one-half hour with about 5 g. of freshly dehydrated lime (Note 8). After filtering again and washing the lime with a little ether, the ether is distilled and the alcohol is distilled in vacuo from a Claisen flask (Note 9). The carbinol distils at 88–93°/18 mm. (practically all distilling at 91°). The yield is 70–74 g. (61–65 per cent of the theoretical amount) (Note 10).

## 2. Notes

1. If the cyclohexyl bromide contains traces of alcohol the yield is considerably reduced. The alcohol may be removed by washing with cold concentrated sulfuric acid, then with water, and finally drying and distilling.

2. Since a considerable amount of formaldehyde repolymerizes on the walls of the side tube, a wide tube is used to prevent clogging. Clogging by deposition of the reaction product is reduced by having the entry tube about 1 cm. above the surface of the solution.

3. Vigorous stirring is desirable as it materially affects the rate of absorption of the gaseous formaldehyde.

4. The amount of paraformaldehyde used is considerably in excess of one mole since it is difficult to tell when the reaction is complete because of repolymerization. For larger runs, the amount of paraformaldehyde need not be increased in direct proportion, as the 20-g. excess used here is sufficient to insure complete reaction in a run of almost any size. An excess of formaldehyde apparently does not decrease the yield.

5. If paraformaldehyde is used directly without depolymerization, the yield is only 40–45 per cent.

6. At the end of about one and one-half hours tests are made at fifteen-minute intervals for the presence of Grignard reagent. The reaction need not be interrupted. About a one-half cc. sample is pipetted out for each test. To this is added an equal volume of a 1 per cent solution of Michler's ketone in dry benzene. The reaction product is then hydrolyzed by the slow addition of 1 cc. of water. The subsequent addition of several drops of a 0.2 per cent solution of iodine in glacial acetic acid develops a characteristic greenish-blue color when Grignard reagent is present. The reaction is complete when no positive test is obtained for the Grignard reagent (*J. Am. Chem. Soc.* **47**, 2002 (1925)).

7. The ice must be added all at once so that the mixture stays cold at all times and does not become too hot at any one spot. If this happens, the reaction becomes very vigorous, and the mixture is likely to foam out of the flask.

8. The heating with freshly dehydrated lime not only removes traces of water, but gives a product which is entirely free from halogen.

9. It is advisable to use a flask with fractionating side arm (Org. Syn. **1**, 40).

10. If cyclohexyl chloride is used the yield is 68–70 g. (59.5–61 per cent of the theoretical amount).

### 3. Other Methods of Preparation

Cyclohexylcarbinol has been prepared by the reduction of ethyl hexahydrobenzoate with sodium and alcohol,[1] and by

heating an ether solution of cyclohexylmagnesium bromide or chloride with paraformaldehyde.[2]

[1] Compt. rend. **137**, 60 (1903); Ger. pat. 164,294.

[2] Bull. soc. chim. (3) **32**, 574 (1904); Compt. rend. **139**, 343 (1904); Bull. soc. chim. (3) **35**, 544 (1906); Ber. **40**, 4863 (1907).

## 3-CYCLOHEXYLPROPINE-1

$$C_6H_{11}CH_2CBr{=}CH_2 + NaNH_2 \rightarrow C_6H_{11}CH_2C{\equiv}CH + NaBr + NH_3$$

Submitted by R. Lespieau and M. Bourguel.
Checked by Roger Adams and M. M. Brubaker.

### 1. Procedure

A mixture of 120 g. (3 moles) of sodamide (Note 1) and 200 cc. of purified mineral oil (Note 2) is ground together in a mortar until the amide is finely pulverized (Note 3). This suspension is transferred to a 2-l. round-bottom, three-necked flask fitted with a reflux condenser holding a calcium chloride tube, a 500-cc. separatory funnel, and an efficient mechanical stirrer through a mercury seal. The mortar and pestle are rinsed with an additional 250 cc. of the oil which is then added to the reaction flask. This is heated in an oil bath maintained at 160–165°, the stirrer is started and 203 g. (1 mole) of cyclohexylbromopropene (p. 20) is dropped in during one and one-half hours. Ammonia is evolved and this is allowed to pass through the condenser and is collected in water.

After all of the cyclohexylbromopropene has been run in, heating is continued for about two hours, the mixture is cooled and 500 cc. of ether is added. This mixture is poured on 1.5 kg. of cracked ice in a 5-l. flask and then acidified with 280 cc. of concentrated hydrochloric acid. The ether layer is separated, dried over calcium chloride and transferred to a 1-l. modified Claisen flask (Org. Syn. **1**, 40) for distillation. The ether is distilled at ordinary pressure and then the cyclohexylpropine under diminished pressure. The product boiling up to 115°/20

mm. is collected and fractionated. The cyclohexylpropine boils at 58–63°/20 mm. The higher-boiling material is chiefly unchanged cyclohexylbromopropene which may be used again in a subsequent run. The yield of cyclohexylpropine is 80 g. (66 per cent of the theoretical amount not taking into consideration the recovered cyclohexylbromopropene which amounts to about 10 g.) (Note 4). The pure compound boils at 61–63°/24 mm.

## 2. Notes

1. The sodamide must be free from sodium hydroxide and may be conveniently weighed under the 250 cc. of purified mineral oil which is used to rinse out the mortar. Care must be exercised in the use of old sodamide as it sometimes contains an explosive compound that might cause trouble. The nature of this explosive compound is not definitely known; however, it appears to be associated with the development of a lemon yellow color. Should any part of the sodamide develop this color it is recommended that the whole be destroyed at once.

2. Any clean, high-boiling petroleum oil may be used. None of it should boil below 250°.

3. It is essential that the sodamide be very finely divided. The state of subdivision of the sodamide particles seriously affects the yield of product. A mechanical grinder was used by the original authors who obtained better yields than those reported here.

4. By a similar procedure decine-1 may be made from 2-bromodecene-1 in 68 per cent yield, b.p. 80–82°/22 mm., and 4-phenylbutine-1 from 4-phenyl-2-bromobutene-1 in 60 per cent yield, b.p. 95–99°/17 mm.

## 3. Other Methods of Preparation

3-Cyclohexylpropine-1 has been prepared in a pure state only by the action of sodamide on cyclohexylbromopropene.[1]

[1] Ann. chim. (10) **3**, 231 (1925). See also, Bull. soc. chim. (4) **7**, 433 (1910).

# X

## DIACETONAMINE HYDROGEN OXALATE

$$CH_3COCH{=}C(CH_3)_2+NH_3 \rightarrow CH_3COCH_2C(CH_3)_2NH_2$$

$$CH_3COCH_2C(CH_3)_2NH_2+H_2C_2O_4+H_2O \rightarrow CH_3COCH_2C(CH_3)_2NH_2\cdot H_2C_2O_4\cdot H_2O$$

Submitted by P. R. HAESELER.
Checked by ROGER ADAMS and G. S. HIERS.

### 1. Procedure

A MIXTURE of 200 g. (2 moles) of mesityl oxide (Org. Syn. **1**, 53) and 280 cc. of aqueous ammonia (27 per cent) is placed in a 1-l. round-bottom flask which is equipped with an efficient mechanical stirrer. The stirrer should be inserted through a stopper in such a way that the flask is nearly air-tight. Because of the heat generated during the reaction it is desirable to keep tap water running over the flask. After stirring for several hours (Note 1) the system becomes homogeneous. When this point is reached the stirring is discontinued, and the well-stoppered flask is allowed to stand at room temperature for three days (Note 2).

Dry air is blown through the solution to remove the excess of ammonia, and the solution is then dissolved in its own volume of absolute alcohol. A sample of this solution is titrated with standard oxalic acid, litmus being used as an outside indicator (Note 3). The amount of oxalic acid (Note 4) necessary to form the acid salt is placed in a large evaporating dish and dissolved in 4 l. of 95 per cent alcohol. The amine solution is then slowly run into the acid with constant stirring. During the addition of the last half of the amine solution, the container must be cooled in order to avoid the formation of the neutral oxalate.

The resulting mixture is then heated on a steam cone or an air bath with constant stirring until the temperature of the mixture reaches 70°. The mixture is filtered, while hot, through a previously heated Büchner funnel. The filtrate is immediately placed in a large beaker or evaporating dish for the crystallization of the diacetonamine hydrogen oxalate (Note 5). The residue is treated with boiling alcohol and filtered, the filtrate containing a small additional quantity of the amine hydrogen oxalate. The mother liquor is distilled until nothing further passes over at 78° (Note 6), and the residue is allowed to stand for a day in a cool place. The crystals that separate are washed with cold absolute alcohol and dried. A total yield of 285–320 g. (62–70 per cent of the theoretical amount) of product that melts at 126–127° is obtained (Note 7).

## 2. Notes

1. The time required varies between three and eight hours, and the lower time limit is very materially favored when the reaction is carried out in the sunlight.

2. The period of three days seems to be the most desirable length of time to allow the reaction mixture to stand; the reaction is not complete in less time and the yields tend to become smaller if a much longer time is employed.

3. The volume of the diluted amine is usually between 800 and 860 cc. A 10-cc. portion of this may be conveniently drawn off with a pipette and usually requires from 35 to 50 cc. of 0.5 N oxalic acid.

4. The end point to litmus occurs when the neutral salt is formed. As the acid salt is desired, twice the amount of oxalic acid calculated above is used. This is usually between 230 and 260 g.

5. If the crystals are allowed to remain in contact with the mother liquor for several hours without filtering, they become somewhat dark in color. This color may be removed by washing with hot absolute alcohol.

6. The alcohol recovered in this way may be used as a solvent

in subsequent runs. When about 3.5 l. of alcohol has been distilled, the residue gives a small yield (10–15 g.) of dark crystals which must be washed several times with warm absolute alcohol to remove most of the color.

7. The product is entirely free from triacetonamine, triacetondiamine and other troublesome condensation products, thus making its purification very simple. There is, however, a small quantity of ammonium hydrogen oxalate mixed with this salt to the extent of 1–1.2 per cent, but since it offers no difficulty when the product is used for synthetic purposes it is usually ignored. A small amount of ammonium salt has practically no effect on the melting point. It is possible to get pure diacetonamine hydrogen oxalate by recrystallizing from absolute alcohol.

## 3. Other Methods of Preparation

Diacetonamine has been prepared in satisfactory yields by treating a mixture of commercial acetone and calcium chloride with anhydrous ammonia.[1] The preparation from commercial acetone and ammonia is laborious and gives low yields.[2] No yields are given in the older published descriptions of the preparation from mesityl oxide with either aqueous or anhydrous ammonia.[3] The method described here has recently been published.[4]

[1] J. Chem. Soc. **115**, 588 (1919).
[2] Ann. **174**, 136 (1874); **189**, 214 (1877).
[3] Ber. **7**, 1387, 1776 (1874).
[4] J. Am. Chem. Soc. **47**, 1195 (1925).

XI

## $\alpha$, $\alpha$-DIPHENYLETHYLENE

$$2C_6H_5MgBr + CH_3CO_2C_2H_5 \xrightarrow{H_2O}$$
$$CH_3(C_6H_5)_2COH + Mg(OH)Br + Mg(OC_2H_5)Br$$
$$CH_3(C_6H_5)_2COH \rightarrow (C_6H_5)_2C{=}CH_2 + H_2O$$

Submitted by C. F. H. ALLEN and S. CONVERSE.
Checked by HENRY GILMAN and N. J. BEABER.

### 1. Procedure

IN a 2-l. three-necked flask, fitted with a separatory funnel, reflux condenser and stirrer, is placed 27 g. (1.1 moles) of magnesium turnings. A mixture of 30 g. of bromobenzene and 70 cc. of dry ether is run in and the flask warmed gently with a free flame until the reaction becomes rapid. Stirring is then started and the vessel is surrounded by a dish of cold water. A mixture of 151 g. of bromobenzene (total: 181 g., 1.15 moles) and 380 cc. of dry ether is run in at such a rate as to cause vigorous refluxing; when the addition is complete (one hour) the whole is stirred for ten minutes.

After the flask has been cooled by immersion in ice water, 44 g. (0.5 mole) of dry ethyl acetate (Note 1) in an equal volume of ether is added over a period of twelve minutes. The cooling bath is removed and stirring is continued for ten minutes. When the reaction flask has again been cooled by the ice-water bath, a previously prepared ammonium chloride solution (Note 2) is added, very slowly at first, over a period of ten minutes, during which a pasty solid separates.

The ether layer is decanted into a separatory funnel. To this is added a 50-cc. ether extract of the pasty residue, and the

combined ether solutions are dried by shaking with anhydrous calcium chloride. The solvent is best removed by dropping into a 250-cc. Claisen flask attached to a condenser, and immersed in an oil bath heated at 210–215°. After the ether has distilled, the flask is heated for half an hour, and then the pressure is reduced to about 30 mm., the bath temperature being maintained at about 210° (Note 3). At first a low-boiling fraction consisting of bromobenzene (12–14 g.) and traces of water distil, after which the diphenylethylene comes over as a colorless liquid, the last portions being slightly yellowish. The brownish residue contains polymerization and decomposition products. On redistillation, the pure hydrocarbon boils at 113°/2 mm. (Note 4). The yield is 60-66 g. (67–70 per cent of the theoretical amount based on ethyl acetate (Note 5)).

## 2. Notes

1. The grade of ethyl acetate used is very important. If ordinary ethyl acetate is used it may be purified by washing with twice its volume of water, drying over fused potassium carbonate, refluxing with phosphorus pentoxide, filtering, and fractionating, whereupon practically all comes over at constant temperature. The addition to the Grignard reagent should be cautious at first, to avoid a vigorous reaction that frequently occurs after about 15 cc. has been added.

2. The ammonium chloride solution is prepared by dissolving 50 g. of ammonium chloride in 150 cc. of water at 25–30°. The literature recommends the use of 30 per cent sulfuric acid for decomposing the magnesium compound; when this is used, the yield drops to 50–55 per cent, probably owing to the ready polymerization of the hydrocarbon in the presence of mineral acids.

3. This heating prior to distillation obviates the necessity of intermediate isolation of the carbinol. The dehydration is evidenced by small explosions when the water drops on the hot reaction mixture.

4. The hydrocarbon is reported to boil at 123–5°/5 mm.; 134°/10 mm.[5]; 139°/11 mm.[6]; 156°/25 mm.[4]; 164°/34 mm.[4]; and at 277°/760 mm.[1]

5. The yield is decreased by about 10 per cent if only an equivalent molecular quantity of phenylmagnesium bromide is used.

### 3. Other Methods of Preparation

$\alpha,\alpha$-Diphenylethylene has been prepared by the action of alcoholic potash on unsymmetrical diphenylchloroethane;[1] by the action of aluminium chloride on a mixture of benzene and acetylene tetrabromide[2] or 1,1-dibromoethylene.[3] The carbinol (from which the hydrocarbon is prepared by dehydration) has always been obtained from the Grignard reaction, either by the action of methylmagnesium iodide on benzophenone,[4, 5, 6, 7] or phenylmagnesium bromide on acetophenone[8] or ethyl acetate.[9, 10] The preparation from ethyl acetate appears to be the cheapest and most convenient method, and the method used is adapted from that previously described by Stadnikov.[10]

[1] Ber. **7**, 1409 (1874).
[2] Ann. **235**, 150, 299 (1886).
[3] Ber. **12**, 2245 (1879).
[4] Ber. **35**, 2646 (1902).
[5] Ber. **56**, 2349 (1923).
[6] Ber. **56**, 567 (1923).
[7] J. Am. Chem. Soc. **45**, 554 (1923).
[8] J. prakt. Chem. (2), **87**, 289 (1913).
[9] Ber. **54**, 1856 (1921).
[10] J. Russ. Phys. Chem. Soc. **47**, 2037, 2115 (1915) (C. A. **1916**, 1355).

# XII

## ETHYL ACETOACETATE

$$2CH_3CO_2C_2H_5 + Na \rightarrow CH_3C(ONa) = CHCO_2C_2H_5 + C_2H_5OH + (H)$$

$$CH_3C(ONa) = CHCO_2C_2H_5 + CH_3CO_2H \rightarrow CH_3COCH_2CO_2C_2H_5 + CH_3CO_2Na$$

Submitted by J. K. H. Inglis and K. C. Roberts.
Checked by C. S. Marvel and F. E. Kendall.

### 1. Procedure

In a 2-l. round-bottom flask, fitted with an efficient reflux condenser, is placed 500 g. (5.7 moles) of ethyl acetate (Note 1), and 50 g. (2.2 moles) of clean sodium wire or finely sliced sodium (Note 2) is added. The reaction is at first quite slow, and must be started by warming on a water bath (Note 3). After the reaction is once started it proceeds vigorously and cooling is then necessary in order to avoid loss of material through the condenser. When the rapid reaction slows down, the reaction mixture is heated on a water bath until the sodium has completely dissolved. This usually requires about one and one-half hours. At this stage the reaction mixture should be a clear red liquid with a green fluorescence.

This solution is then cooled and made slightly acid by adding about 275 cc. of 50 per cent acetic acid (Note 4). Salt is added if necessary to cause the ester to separate. The ester layer is separated, dried over calcium chloride and fractionally distilled under reduced pressure from a modified Claisen flask (Org. Syn. 1, 40).

The yield of ester boiling at 76–80°/18 mm. is 105–110 g. (28–29 per cent of the theoretical amount based on the ethyl acetate) (Note 5).

## 2. Notes

1. The grade of ethyl acetate used is very important. It must be entirely free from water and should contain about 2–3 per cent of alcohol. The absolute ethyl acetate of the U. S. Industrial Alcohol Company is satisfactory for use. If this grade is not available, ordinary ethyl acetate may be purified by washing it with twice its volume of water and drying over fused potassium carbonate, from which it is decanted, and used directly. The ethyl acetate purified in this way contains enough ethyl alcohol to allow the reaction to run well. The ethyl acetate in the wash water may be recovered by distilling through a short column from a steam cone until the vapors reach a temperature of 72°. Dry ethyl acetate containing 2-3 per cent of alcohol has a boiling point range of 2 to 3°.

If the ester is dry enough to use in this reaction it will not give a gelatinous mass of sodium hydroxide when treated with a little sodium.

2. Sodium wire and finely sliced sodium are equally good to use in this reaction. It is important to avoid contamination of the sodium by surface action which converts part of it into sodium hydroxide.

3. It is convenient to arrange the water bath so that it may be heated by passing in steam or cooled by running in cold water.

4. It is advisable to avoid a large excess of acetic acid since it increases the solubility of the ester in water.

5. When larger runs are made the yields increase; thus 2000 cc. of ethyl acetate and 200 g. of sodium give 515–568 g. of ethyl acetoacetate. From a run of this size it is possible to recover about 700 cc. of ethyl acetate. Approximately a proportionate recovery is obtained in smaller runs.

The yield is based on ethyl acetate and not on sodium, because it is uncertain whether one or two moles of sodium react with one mole of ethyl acetate.

### 3. Other Methods of Preparation

Ethyl acetoacetate has been prepared from ethyl acetate by the action of sodium,[1] sodium ethylate,[2] sodamide,[3] and calcium.[4]

[1] Jahresber. **1863**, 323; **1865**, 302; Z. Chem. **1866**, 5; Ann. **186**, 214 (1877); J. prakt. Chem. (2) **65**, 528 (1902); Ber. **38**, 709 (1905); Am. Chem. J. **40**, 76 (1908); J. Am. Chem. Soc. **30**, 1876 (1908); U. S. pat. 1,425,626 (C. A. **1922**, 3314); U. S. pat. 1,472,324 (C. A. **1924**, 400); J. Soc. Chem. Ind. **43**, 295 T (1924).

[2] Z. Chem. **1868**, 653; Ber. **33**, 3735 (1900); **38**, 709 (1905); Am. Chem. J. **37**, 299 (1907).

[3] J. Chem. Soc. **81**, 1527 (1902); Ber. **35**, 2321 (1902).

[4] J. Chem. Soc. **95**, 161 (1909).

XIII

# ETHYL ACETOPYRUVATE

$$C_2H_5O_2CCO_2C_2H_5 + CH_3COCH_3 + C_2H_5ONa \rightarrow CH_3COCH{=}C(ONa)CO_2C_2H_5 + 2C_2H_5OH$$

$$CH_3COCH{=}C(ONa)CO_2C_2H_5 + H_2SO_4 \rightarrow CH_3COCH_2COCO_2C_2H_5 + NaHSO_4$$

Submitted by C. S. MARVEL and E. E. DREGER.
Checked by FRANK C. WHITMORE and GLADYS E. WOODWARD.

## 1. Procedure

IN a 5-l. round-bottom flask fitted with a reflux condenser, a mechanical stirrer (Note 1) and a 1-l. separatory funnel, is placed 2800 cc. of absolute ethyl alcohol (Note 2), and to this is added 125 g. (5.4 moles) of sodium over a period of one to two hours. The stirrer is started and the mixture allowed to cool to room temperature (Note 3), and a mixture of 730 g. (5 moles) of ethyl oxalate (Note 4) and 290 g. (5 moles) of acetone (Note 5) is added slowly over a period of two to three hours. At first a white precipitate forms; this is followed by a yellow precipitate that darkens as the reaction proceeds and later turns yellow again. The temperature rises to about 40°. Toward the end the mixture becomes so thick that stirring is difficult. Stirring is continued for one hour after the addition of the oxalate and acetone mixture. The yellow sodium salt is filtered by suction on two 20-cm. Büchner funnels (Note 6). The reaction flask is rinsed with 200 cc. of absolute ethyl alcohol, which is then used to wash the salt. The filtrate is turbid as a rule, but there is not enough sodium salt in suspension or solution to warrant recovery.

When the sodium salt has been sucked dry, it is returned to the 5-l. flask and treated with 1.5 l. of water and 1 kg. of cracked ice.

The stirrer is started and there is added rapidly a cold sulfuric acid solution made by adding enough ice to 200 cc. of concentrated sulfuric acid (sp. g. 1.84) (Note 7) so that some of the ice is not melted. The stirring is continued for five or ten minutes or until the yellow lumps of the sodium salt disappear. The mixture is then extracted with three 600-cc. portions of benzene (Note 8). The benzene is distilled (Note 9) from the extracts on a water bath and the residue is transferred to a special 2-l. Claisen flask (Org. Syn. **1**, 40) and distilled under diminished pressure. The product boils at 130–132°/37 mm. or 117–119°/29 mm. A small high-boiling fraction is redistilled to yield 20–30 g. more of the ethyl acetopyruvate. The total yield is 480–520 g. (61–66 per cent of the theoretical amount).

## 2. Notes

1. The stirrer used is a bent glass rod which nearly scrapes the sides of the flask. A simple paddle stirrer is not efficient enough to stir the semi-solid mass.

2. The quality of the absolute alcohol (Org. Syn. **5**, 56) influences the yields decidedly. The amount of alcohol indicated is the smallest which can be used effectively.

3. No better yields were obtained at lower temperatures.

4. The ethyl oxalate used was dried over calcium chloride for a week (Org. Syn. **2**, 23; **5**, 59).

5. The acetone used was commercial acetone dried over calcium chloride for a week and then distilled.

6. The filtration is likely to be slow and may take as much as two or three hours. When a 40-cm. Büchner funnel was used, it was complete in less than one hour.

7. This is enough acid to turn Congo Red paper distinctly blue. If less acid is used, a troublesome emulsion is likely to form. If such an emulsion forms it can be broken by pouring into it a small amount of sulfuric acid cooled by the addition of ice.

8. If less than 600-cc. portions of benzene are used, the danger of emulsion formation is greater.

9. About 1 l. of benzene is recovered.

## 3. Other Methods of Preparation

Ethyl acetopyruvate has been prepared only by the condensation of ethyl oxalate and acetone in the presence of sodium ethylate.[1] The method given above is based on that of Claisen and Stylos.[2]

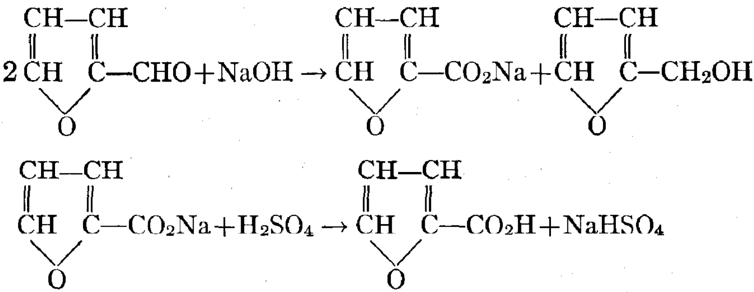
[1] Ber. **20**, 2189 (1887); Ger. pat. 43,847; Winther, I, 98 (1887); Ger. pat. Anmeldung, F. 3,299; Frdl. **1**, 218 (1888); J. Phys. Chem. **12**, 4 (1908); J. Chem. Soc. **95**, 1896 (1909).

[2] Ber. **20**, 2188 (1887).

XIV

# 2-FURANCARBOXYLIC ACID and 2-FURYLCARBINOL

(Pyromucic or Furoic Acid) (Furfuryl Alcohol)



Submitted by W. C. Wilson.
Checked by C. S. Marvel and C. G. Gauerke.

## 1. Procedure

One kilo (10.4 moles) of furfural (Note 1) is placed in a 4-l. copper can (Note 2) provided with a mechanical stirrer and surrounded by an ice bath. The stirrer is started and the furfural is cooled to 5–8°. When the temperature has fallen to this range, 825 g. of 33.3 per cent technical sodium hydroxide solution (Note 3) is added from a separatory funnel at such a rate that the temperature of the reaction mixture does not exceed 20°. This requires twenty to twenty-five minutes. The rate of addition will depend on the efficiency of the cooling. The stirring is continued for one hour after the addition of the sodium hydroxide solution.

During the reaction considerable sodium 2-furancarboxylate separates in fine scale-like crystals. The reaction mixture is allowed to come to room temperature and just enough water is added to dissolve this precipitate. This requires about 325 cc.

The solution is then placed in a continuous extraction apparatus (Org. Syn. **3**, 88) and the 2-furylcarbinol is extracted with 1500–2000 cc. of ether (Note 4). The extraction is complete after six to seven hours.

When extraction is complete the ether solution of 2-furylcarbinol is distilled until the temperature of the liquid (not the vapor) reaches 95°. Then the residue is distilled under diminished pressure. Some ether and water come over first and the temperature then rises rapidly to the boiling point of 2-furylcarbinol. The yield of 2-furylcarbinol boiling at 75–77°/15 mm. is 310–325 g. (61–63 per cent of the theoretical amount) (Note 5).

The water solution containing the sodium 2-furancarboxylate is made acid to Congo Red paper with 40 per cent sulfuric acid. This requires about 400 cc. On cooling, the 2-furancarboxylic acid crystallizes and is filtered with suction. The crude acid contains considerable sodium hydrogen sulfate and is deeply colored. For purification it is dissolved in 2300 cc. of boiling water containing about 60 g. of decolorizing carbon (Norite) and the solution is boiled for about forty-five minutes. It is then filtered and cooled with stirring to 16–20° (Note 6) and the 2-furancarboxylic acid which crystallizes is filtered by suction. The product thus obtained is light yellow in color but darkens somewhat on standing. The yield is 360–380 g. (51–54 per cent of the theoretical amount) (Note 7). This acid melts at 121–124° and by titration is 93–95 per cent pure. It is pure enough for many purposes.

For further purification the material may be recrystallized from hot water, or dissolved in alkali and reprecipitated, or distilled under reduced pressure or sublimed. Each of these operations involves considerable loss of product, either through solubility or through decomposition by heat. The best-appearing product is obtained by distillation under reduced pressure. The crude acid is distilled from a Claisen flask with a delivery tube set low in order that the acid need not be heated much above the boiling point. The product boiling at 141–144°/20 mm. is pure white and melts at 125–132° (Note 8). The yield of distilled acid is about 75–85 per cent of the weight of the crude acid.

## 2. Notes

1. Technical furfural (sp. g. 1.15) was used in this preparation. It boiled over a range of 140–160° and contained about 2 per cent water.

2. A one-gallon ice-cream freezer is a very convenient apparatus to use for the reaction.

3. This amounts to about 28 per cent pure sodium hydroxide or 5.77 moles.

4. Carbon tetrachloride may be used for the extraction of the 2-furylcarbinol. This requires altering the extraction apparatus to remove the solvent from the bottom of the extraction bottle. Some difficulties are met in working with carbon tetrachloride, due to the liberation of acid which causes the 2-furylcarbinol to change into the water-insoluble form. The yields of both 2-furancarboxylic acid and 2-furylcarbinol are much lower when carbon tetrachloride is used as a solvent.

5. The 2-furylcarbinol thus obtained is entirely soluble in water and has only a slight yellow tinge. If it is to be stored, about 0.5 to 1 per cent of its weight of urea should be added as a stabilizer.

6. If the solution is cooled lower than 16°, sodium hydrogen sulfate ($NaHSO_4 \cdot 10H_2O$) begins to separate with the 2-furancarboxylic acid.

7. The low yields of 2-furancarboxylic acid are due partly to the formation of tarry by-products and partly to loss through water solubility. The mother liquors contain about 2.5 g. of 2-furancarboxylic acid per 100 cc. This may be recovered by extraction with ether.

8. The melting point of the 2-furancarboxylic acid is not very sharp. The distilled acid which titrates 100 per cent softens noticeably at 125° and melts completely at 132°. (Gelissen and van Roon, *Rec. trav. chim.* **43**, 361 (1924)).

## 3. Other Methods of Preparation

2-Furancarboxylic acid may be prepared by the dry distillation of mucic acid,[1] by the oxidation of furfural with potassium

permanganate[2] and by the Cannizzaro reaction from furfural.[3] The last method has been found to be the most satisfactory from a practical standpoint.

2-Furylcarbinol has been prepared by the reduction of furfural with sodium amalgam[4] but the Cannizzaro reaction[5] is the better practical method of preparation.

[1] Ann. chim. phys. (2) **9**, 365 (1818).

[2] Ann. **116**, 259 (1860); **261**, 380 (1891); Bull. soc. chim. (3) **17**, 610 (1897); J. Chem. Soc. **79**, 515, 847 (footnote) (1901).

[3] Jahresber. **1860**, 269; Ann. **165**, 279 (1873); **258**, 119 (1890); **261**, 255 (1891); Am. Chem. J. **3**, 37 (1881–2); **44**, 404 (1910).

[4] Ann. Suppl. **3**, 275 (1864–5).

[5] Jahresber. **1860**, 269; Ann. **165**, 279, 300 (1873); **239**, 374 (1887); **272**, 293 (1892); Bull. soc. chim. (3) **21**, 583 (1899); Ber. **35**, 1855 (1902); J. Am. Chem. Soc. **46**, 2576 (1924).

# XV

## $\alpha$-GLYCERYL PHENYL ETHER

$$C_6H_5ONa+CH_2ClCHOHCH_2OH \rightarrow C_6H_5OCH_2CHOHCH_2OH+NaCl$$

Submitted by T. S. WHEELER and F. G. WILLSON.
Checked by H. T. CLARKE and E. R. TAYLOR.

### 1. Procedure

To 500 cc. of absolute alcohol (Note 1) in a 1-l. flask fitted with a reflux condenser is added gradually 46 g. (2 moles) of sodium in thin slices (Note 2) at such a rate that the mixture boils steadily. When all the sodium has been added, the mixture is heated on the steam bath until the few remaining pieces of sodium barely react. Pure commercial molten phenol is now added gradually through the condenser until all of the sodium has reacted, and then the remainder of 188 g. (2 moles) of phenol is added. This is followed by the addition of 221 g. (2 moles) of redistilled glycerol $\alpha$-monochlorohydrin (Org. Syn. **2,** 33) in small portions, the rather vigorous reaction being allowed to complete itself before each subsequent addition.

When all has been added, the mixture is heated on the steam bath for about one hour. The end of the reaction is determined by withdrawing a sample, filtering it, and heating the filtrate in which little or no precipitate should form. The mixture is filtered hot by suction through filter cloth or heavy filter paper (Note 3), the precipitate being washed with three 50-cc. portions of absolute alcohol. The filtrate and washings are distilled on the steam bath under slightly reduced pressure until no more alcohol comes over; the residue, which sets to a white waxy solid on cooling, is transferred to a distilling flask and distilled under reduced pressure, collecting the fraction boiling at 175–190°/15 mm. In this

way 235–275 g. of a product melting at 43–49° is obtained. On redistillation, 205–215 g. (61–64 per cent of the theoretical amount) of a fraction which boils at 185–187°/15 mm. and melts at 48–53° is obtained (Note 4.)

## 2. Notes

1. Absolute alcohol is required in order that all the sodium chloride formed may be precipitated and that none may remain to contaminate the product.

2. More rapid solution of the sodium can be obtained if the metal be granulated prior to its addition to the alcohol. This is done by covering the sodium with ten times its weight of dry xylene and heating to 120° in a stout round-bottom flask (Nef, *Ann.* **280**, 307 (1894) and Read and Lucarni, *Ind. Eng. Chem.* **17**, 480 (1925)). The flask is then well corked, wrapped in a thick, dry cloth and well shaken for a short time. The metal is thus obtained in the form of small spheres, the size of which is controlled by the time and rapidity of the shaking. A dry bucket should be kept at hand so that the flask can be dropped into it in case of breakage. Not more than 30 g. of sodium should be treated at one time.

Vigorous mechanical stirring may be used to advantage in place of shaking by hand.

3. The precipitate of sodium chloride obtained is very sludgy and filters poorly through fine-fibered papers.

4. Small traces of impurity lower the melting point very considerably, and by repeated recrystallization from anhydrous ether the melting point can be raised to 70°. The product crystallizes from the ether in very long, flexible needles, forming a spongy mass which filters with some difficulty. In order to obtain a high melting point, complete removal of the solvent, preferably by warming to 50° under reduced pressure, is essential.

## 3. Other Methods of Preparation

α-Glyceryl phenyl ether has been prepared by heating phenyl glycide ether in a closed tube with water at 120°:[1] by the action

of benzene diazonium chloride on glycerol at 100°;[2] by heating phenol with excess of glycerol and dehydrated sodium acetate in an inert atmosphere at an elevated temperature;[3] by heating phenol with α-monochlorohydrin and caustic alkali at 100°.[4] None of these methods gives as good a yield as that described above.

[1] Ber. **24**, 2147 (1891); *Cf.* Rec. trav. chim. **34**, 102 (1915).
[2] Ber. **36**, 2064 (1903).
[3] Monatsh. **29**, 952 (1908).
[4] J. Chem. Soc. **101**, 310 (1912).

## XVI

# $n$-HEPTYL ALCOHOL

$$CH_3(CH_2)_5CHO + 2H \rightarrow CH_3(CH_2)_5CH_2OH$$

Submitted by H. T. Clarke and E. E. Dreger.
Checked by C. S. Marvel and L. T. Sandborn.

## 1. Procedure

In a 12-l. flask fitted with a mechanical stirrer and a short reflux condenser are placed 1800 g. (32.2 moles) of iron filings (Note 1), 3 l. (52.5 moles) of glacial acetic acid, 3 l. of water, and 450 g. (3.95 moles) of heptaldehyde (Note 2). The mixture is heated on the steam bath, with stirring, for six to seven hours (Note 3). The flask is then fitted to an apparatus for steam distillation (Org. Syn. **2**, 80) and the mixture distilled in a current of steam (Note 4) until no more oil passes over (7–8 l. of distillate). The oil is then separated, and the aqueous part distilled to recover a small quantity of dissolved or suspended heptyl alcohol.

The combined product is mixed with 1 l. of 20 per cent sodium hydroxide solution and stirred on the steam bath for four hours, in order to hydrolyze a small proportion of heptyl acetate. The oil is then separated and distilled, and the portion boiling at 172–176° collected. The residue in the flask is mixed with about 100 cc. of water and distilled, whereupon a further small quantity of oil passes over with the steam. This distillate and the forerun are freed of the bulk of the water in a separatory funnel, and distilled from a smaller flask. In this way the total yield of $n$-heptyl alcohol boiling at 172–176° (uncorr.) is 350–370 g. (75–81 per cent of the theoretical amount). The alcohol may be redistilled under reduced pressure, and it passes over almost without loss at 71–72°/12 mm.

## 2. Notes

1. The iron filings used were free of grease and ore. Ninety-five per cent of the filings passed an 80-mesh screen and 60 per cent passed a 100-mesh screen. Grade "D" iron supplied by the Master Builders Company, Cleveland, Ohio, is ready for use and very satisfactory.

2. The heptaldehyde should be a freshly distilled product, boiling at 154–156°.

3. The reaction may be successfully carried out without a stirrer, but the time of heating must then be lengthened to twelve to fifteen hours.

4. It is advisable to begin the steam distillation at once, while the mixture is hot, and to avoid the use of a free flame, which might cause breakage of the flask. If foaming, or too great a volume, hinders a rapid distillation, it is well to decant part of the contents of the flask and to conduct the steam distillation in two portions.

## 3. Other Methods of Preparation

Heptyl alcohol has been prepared by the reduction of heptaldehyde with zinc dust and acetic acid,[1] with sodium amalgam and acetic acid,[2] with sodium in toluene and acetic acid,[3] and with hydrogen and a platinum catalyst.[4] Heptaldehyde has also been reduced biochemically by adding it to a fermenting sugar solution.[5] Heptyl alcohol has been prepared by the reduction of heptoamide with sodium and amyl alcohol.[6]

The above method is based on a process described by A. J. Hill and Edith H. Nason[7] for the reduction of cinnamaldehyde.

[1] Ann. **124**, 352 (1862); *cf.* Ber. **16**, 1723 (1883).
[2] Ann. **177**, 303 (1875); **189**, 2 (1877); **200**, 102 (1880).
[3] J. Biol. Chem. **35**, 281 (1918).
[4] J. Am. Chem. Soc. **45**, 1076 (1923).
[5] Biochem. Zeit. **59**, 183 (1914).
[6] Monatsh. **25**, 1087 (1904).
[7] J. Am. Chem. Soc. **46**, 2236 (1924).

## XVII

# $n$-HEXYL ALCOHOL

$$CH_3(CH_2)_2CH_2Br + Mg \rightarrow CH_3(CH_2)_2CH_2MgBr$$

$$CH_3(CH_2)_2CH_2MgBr + \underset{\diagdown\, O \,\diagup}{CH_2{-}CH_2} \rightarrow$$

$$CH_3(CH_2)_4CH_2OMgBr \xrightarrow{H_2O} CH_3(CH_2)_4CH_2OH$$

Submitted by E. E. Dreger.
Checked by Roger Adams and G. S. Hiers.

## 1. Procedure

In a 5-l. round-bottom flask, fitted with a stirrer, separatory funnel and a reflux condenser to the upper end of which a calcium chloride tube is attached, is placed 150 g. of magnesium turnings. A small crystal of iodine (Note 1) and about 100 cc. of a mixture of 822 g. (6 moles) of $n$-butyl bromide and 2 l. of anhydrous ethyl ether are added. As soon as the reaction starts, 350 cc. of anhydrous ether is added and the remainder of the $n$-butyl bromide solution is dropped in at such a rate that the mixture boils continuously. The time of addition (one and one-half hours) may be decreased by cooling the flask externally. Stirring is started as soon as enough liquid is present in the flask.

When all has been added (Note 2), 278 g. (6.3 moles) of ethylene oxide (Note 3) (previously dried with soda lime) is added through a tube (3 or 4 mm. in diameter) the end of which is about 20 mm. above the surface of the liquid (Note 4), the temperature being kept below 10° by cooling in an efficient ice-and-salt bath (Note 5). This addition requires four to six hours. When all has

been added the ice bath is removed; the temperature of the mixture generally rises enough to cause gentle boiling. When this ceases the mixture is warmed on a steam bath for one hour longer.

The condenser is then arranged for downward distillation, and when about 1 l. of ether has distilled (Note 6) the receiver is changed and 1 l. of dry benzene (Note 7) is added; distillation is continued with stirring until the temperature of the distilling vapor reaches 65°. The mixture is then boiled under reflux for one hour. Usually by this time it has become so viscous that stirring is no longer efficient. The mixture is then allowed to cool and is decomposed with 2 l. of an ice-water mixture. The precipitated magnesium hydroxide is dissolved by adding a sufficient quantity of 30 per cent sulfuric acid and enough ice to keep the mixture cold.

The mixture of benzene and hexyl alcohol is now distilled in a current of steam; about 7 l. of distillate must be collected before all of the product is distilled. The oily layer is separated and the watery portion distilled until free of hexyl alcohol. The oil so obtained is added to the main quantity and the watery portion again distilled. The united product is now stirred on the steam bath for one to two hours with 1 l. of 20 per cent sodium hydroxide solution and again subjected to steam distillation, as before. The oily product so obtained is then distilled under atmospheric pressure with the use of a good fractionating column. The fraction boiling up to 85° is mostly benzene and water. The fraction boiling between 85° and 154° is collected separately for redistillation, and the fraction boiling at 154–157° collected as pure material. There is practically no high-boiling residue. The yield (Note 7) is 368–380 g. (60–62 per cent of the theoretical amount) (Note 8).

## 2. Notes

1. The reaction between the ethereal solution of butyl bromide and the magnesium frequently starts without any assistance, but the presence of a trace of iodine is of no disadvantage and renders more certain the beginning of the reaction.

2. The butyl bromide appears to react as fast as it is added, so that there is no need of stirring or warming the butylmagnesium bromide solution before adding the ethylene oxide. The small amount of unattacked magnesium has no influence on the subsequent reactions.

3. A convenient arrangement consists of placing the ethylene oxide tank on suitable scales and noting the proper decrease in weight. The gas may be passed through a short tower filled with soda lime and then through a spiral condenser surrounded with salt and ice.

4. If the mouth of the delivery tube is beneath the surface, troublesome clogging occurs.

5. The first reaction appears to consist of the formation of an oxonium addition product of the ethylene oxide and the butylmagnesium bromide.

6. Careful watching is necessary at this point, since if the distillation is carried too far a violent reaction, apparently a rearrangement of the initial addition product may set in.

7. By the use of benzene as a diluent the reaction referred to in Note 6 takes place smoothly and without violence; without it the yield is only about 200 g.

8. Instead of adding the condensed ethylene oxide, it may be dissolved in 350 cc. of chilled anhydrous ether which is added during the course of one to two hours. In this case, however, the yields are lower, apparently owing to the vaporization of some of the ethylene oxide.

### 3. Other Methods of Preparation

*n*-Hexyl alcohol has been prepared by the reduction of ethyl caproate by means of sodium and absolute alcohol[1] alone or in anhydrous ammonia solution;[2] by the reduction of *n*-caproamide by means of sodium and absolute alcohol;[3] by the reduction of *n*-caproaldehyde by means of sodium amalgam in dilute sulfuric acid;[4] and by means of living yeast.[5] It has also been produced by the action of nitrous acid upon *n*-hexylamine;[6] by the action of sodium upon a mixture of ethyl alcohol and *n*-butyl alcohol;[7]

and by the interaction of *n*-propylmagnesium bromide and trimethylene oxide,[8] benzene being employed as a diluent as in the foregoing directions.

[1] Bull. sci. acad. roy. Belg. **158**, 77 (1905) (Chem. Zentr. **1905, II**, 214); Bull. soc. chim. (3) **33**, 826 (1905); Ger. pat. 164,294 (Chem. Zentr. **1905, II**, 1700).

[2] Compt. rend. **156**, 1020 (1913).

[3] Compt. rend. **138**, 149 (1904).

[4] Ann. **187**, 135 (1877).

[5] Biochem. Zeit. **67**, 26 (1914) (Chem. Zentr. **1915, I**, 618).

[6] Ber. **16**, 744 (1883).

[7] J. Chem. Soc. **117**, 334 (1920).

[8] J. Am. Chem. Soc. **38**, 2484 (1916).

XVIII

## MANDELIC ACID

$$C_6H_5CHO + NaHSO_3 \rightarrow C_6H_5CHOHOSO_2Na$$

$$C_6H_5CHOHOSO_2Na + NaCN \rightarrow C_6H_5CHOHCN + Na_2SO_3$$

$$C_6H_5CHOHCN + HCl + 2H_2O \rightarrow C_6H_5CHOHCO_2H + NH_4Cl$$

Submitted by B. B. CORSON, RUTH A. DODGE, S. A. HARRIS and J. S. YEAW.
Checked by C. S. MARVEL and M. M. BRUBAKER.

### 1. Procedure

IN a 4-l. wide-mouthed glass jar, fitted with a mechanical stirrer, is placed a solution of 150 g. (3 moles) of sodium cyanide (Note 1) in 500 cc. of water and 318 g. (3 moles) of U.S.P. benzaldehyde. The stirrer is started and 850 cc. of a saturated solution of sodium bisulfite (Note 2) is added to the mixture, slowly at first and then in a thin stream. The time of addition is ten to fifteen minutes. During the addition of the first half of this solution, 900 g. of cracked ice is added to the reaction mixture, a handful at a time. The layer of mandelonitrile which appears during the addition of the sulfite solution is separated from the water in a separatory funnel. The water is extracted once with about 150 cc. of benzene, the benzene is evaporated, and the residual mandelonitrile is added to the main portion.

The crude nitrile (about 290 cc.) is placed at once (Note 3) in a 25 cm. evaporating dish, and 425 cc. of C.P. concentrated hydrochloric acid (sp. g. 1.19) is added. The hydrolysis is allowed to proceed in the cold (Note 4) for about twelve hours, after which the mixture is heated on a steam bath to remove the water and excess hydrochloric acid. After heating for five to six hours it is advisable to cool the mixture (Note 5) and

filter the ammonium chloride and mandelic acid mixture that separates. The filtrate is then evaporated to dryness. This residue is added to the solid material obtained before. The product is deeply colored and must be dried in the air and light for at least twenty-four hours. The total yield of the crude mandelic acid-ammonium chloride mixture is 370–390 g., depending on the amount of moisture. The mixture of ammonium chloride and mandelic acid is ground in a mortar, transferred to a 2-l. flask, and washed twice with 750-cc. portions of cold benzene (Note 6). The insoluble portion is transferred to a suction funnel and sucked dry.

Either of two methods may be used to extract the mandelic acid from the ammonium chloride.

A. *Extraction with Benzene.* The mandelic acid is separated from the ammonium chloride by extraction with hot benzene. This is best done by dividing the solid mixture into ten approximately equal parts (Note 7). One of these portions is placed in flask with 1 l. of boiling benzene. After a few minutes the hot benzene solution is decanted through a suction funnel (Note 8). The filtrate is cooled in an ice bath and the mandelic acid that crystallizes is filtered with suction. The benzene is returned to the extraction flask containing the residue from the first extraction, and a new portion of the ammonium chloride-mandelic acid mixture is added and extracted as before. The process is repeated until the mandelic acid is completely removed from the ammonium chloride (Note 9).

The yield of pure white mandelic acid melting at 118° is 229–235 g. (50–52 per cent of the theoretical amount based on benzaldehyde).

B. *Extraction with Ether* (Note 10).—The solid mixture is transferred to a 2-l. flask and shaken ten minutes with 750 cc. of ether. The ether solution is decanted through a suction filter and the solid thrown onto the filter and pressed dry. The solid is then returned to the flask and shaken with 400 cc. of ether. This mixture is filtered by suction and the solid washed twice on the filter with 250 cc. portions of ether. Each portion is allowed to drain through the filter several times while the solid is kept

porous with a spatula. The combined ether filtrate is then filtered through an ordinary funnel (Note 11). The ether solution is placed in a 3-l. round-bottom flask and 750 cc. of toluene (Note 12) is added. The mixture is distilled on a steam bath through an efficient fractionating column as long as it distils easily and about 1100–1400 cc. of distillate is collected. The temperature of the vapor rises to about 70°. The mixture is then heated over a free flame until the temperature in the column is 95°; about 300 cc. distils (Note 13). The residual liquid is poured while still hot into a large beaker immersed in ice water. The liquid (about 900 cc.) is stirred by hand until it has become a thick crystal mush. The cooling is continued for two hours with occasional stirring so as to bring the temperature down to 5–10°. The mixture is filtered with suction and the solid pressed dry. It is then thoroughly washed on the filter with 300 cc. of toluene in several portions (Note 14).

The yield is the same as that obtained by method (A).

## 2. Notes

1. This reaction and the subsequent hydrolysis should be carried out in a good hood as some hydrogen cyanide is liberated. The sodium cyanide used was the technical "cyan-egg," containing about 92–95 per cent of cyanide.

2. This saturated solution is best prepared by stirring 1500 g. of technical sodium bisulfite (97–100 per cent) with 2 l. of water and filtering to remove the excess salt. The specific gravity of this solution is 1.37–1.39.

3. The mandelonitrile should be mixed with hydrochloric acid as soon as it is separated from the water. Wood and Lilley (*J. Chem. Soc.* **127**, 95 (1925)) have found that it undergoes rapid rearrangement to the isonitrile. Hence if it is allowed to stand long before the hydrolysis, the yield of mandelic acid is reduced.

4. The hydrolysis can be carried out in the hot, but the final product may be deeply colored.

5. It is advisable to stir the mixture during the cooling in order to break up the lumps and thus obtain a product that can be more easily filtered.

6. If the crude product is not first washed with cold benzene the final product is usually colored. Very little mandelic acid is lost by this washing.

7. The entire amount of the ammonium chloride-mandelic acid mixture may be boiled with the benzene but this gives a supersaturated solution of the acid in the benzene and much difficulty is met in the filtration. The solubility of mandelic acid in hot benzene is approximately 1 g. in 50 cc.

It may be better to carry out the extraction in a Soxhlet apparatus or an apparatus of the type described in Org. Syn. **2**, 49.

8. The funnel should be previously heated and have fairly large holes so as not to be clogged by the mandelic acid that begins to crystallize as soon as the solution cools slightly. Only a slight suction should be applied during filtration.

9. Usually two or three extractions of the ammonium chloride residues after the addition of the last portion of the crude mixture are necessary in order to obtain all of the mandelic acid. On concentrating the benzene used for the extraction, about 5 g. of impure mandelic acid may be obtained. To diminish mechanical losses it is recommended that the same container be used to collect and crystallize the several filtrates.

10. The ether extraction method (B) is quicker, especially when several runs are to be made. Mandelic acid is obtained in the same yield by this method. The benzene extraction may be better for small preparations, or when a single run is to be made.

11. An occasional water layer should be removed in a separatory funnel.

12. Benzene works almost as well as toluene; xylene can also be used.

13. The temperature in the column is a better guide than the volume of distillate. A few porous chips should be added to prevent bumping. The ether-toluene solution should not stand long before distillation since mandelic acid is apt to separate. The heating with steam and with the free flame should be done quickly since prolonged heating lowers the yield.

14. The mother liquors are worked up for toluene, but it is not profitable to try to recover the small amount of impure mandelic acid which they contain.

### 3. Other Methods of Preparation

Mandelic acid is best prepared by the hydrolysis of mandelonitrile with hydrochloric acid. The mandelonitrile has been prepared from amygdalin,[1] by the action of hydrocyanic acid on benzaldehyde,[2] and by the action of sodium or potassium cyanide on the sodium bisulfite addition product of benzaldehyde.[3]

The method in the procedure differs from any previously described in that the sodium bisulfite addition product of benzaldehyde is prepared in the presence of sodium cyanide and the nitrile is formed immediately.

[1] Ann. **4**, 246 (1832); **18**, 310 (1836); Ber. **16**, 1566 (1883).

[2] Ann. **139**, 299 (1866); **193**, 38 (1878); Ber. **14**, 239 (1881); Rec. trav. chim. **28**, 254 (1909); J. Chem. Soc. **113**, 12 (1918).

[3] Ber. **4**, 980 (1871); Arch. Pharm. **202**, 385 (1873); Ger. pat. 85,230; Frdl. **4**, 160 (1895); Chem. Ztg. **20**, 90 (1896).

XIX

## α-METHYL-*d*-GLUCOSIDE

$$C_6H_{11}O_5OH + CH_3OH \rightarrow C_6H_{11}O_5OCH_3 + H_2O$$

Submitted by B. Helferich and W. Schäfer.
Checked by H. T. Clarke and M. R. Brethen.

### 1. Procedure

Dry hydrogen chloride (Org. Syn. **2**, 30) is passed into 200 g. of anhydrous methyl alcohol (Note 1), with ice cooling and exclusion of moisture, until the increase in weight amounts to 5 g. This solution is then diluted with 1800 g. of methyl alcohol, a 0.25 per cent solution of hydrogen chloride being thus obtained. To this is added 500 g. (2.77 moles) of finely powdered anhydrous *d*-glucose (Note 2), and the mixture boiled under reflux for seventy-two hours, a clear solution being obtained after the first fifteen minutes' boiling. It is well to attach a soda-lime tube to the upper end of the condenser, in order to exclude moisture. The clear pale yellow solution is cooled to 0°, and crystallization induced by scratching or by inoculation with a trace of α-methyl-*d*-glucoside. After standing for twelve hours at 0° the first crop is filtered by suction and washed twice with 100-cc. portions of cold methyl alcohol. The yield is 85–120 g. of a product melting at 165°.

The mother liquor and washings are returned to the flask and again boiled for seventy-two hours under reflux. The liquid is concentrated to 800 cc. and again chilled to 0°, inoculated and allowed to stand at 0° for twenty-four hours. The second crop of glucoside so obtained is filtered by suction and washed with three 100-cc. portions of cold methyl alcohol. This yield is 110–145 g., melting at 164–165°. The mother liquor and washings are combined and concentrated to about 300 cc., chilled to 0°,

and again inoculated and allowed to stand for twenty-four hours. The resulting mush of crystals is diluted with twice its weight of absolute ethyl alcohol, and after standing twenty-four hours at 0°, the third crop of glucoside is filtered (Note 3). This is recrystallized from 2.5 parts of methyl alcohol. The yield is 30–36 g., melting at 164–165°.

The total yield amounts to 260–266 g. (48.5–49.5 per cent of the theoretical amount). The product is contaminated by slight traces of *d*-glucose and possesses a very faint reducing power towards Fehling's solution. For complete purification it is recrystallized (with practically no loss and practically no change in melting point) from five parts of methyl alcohol with the use, if necessary, of decolorizing carbon.

## 2. Notes

1. All of the methyl alcohol used in this preparation must be anhydrous and free of acetone.

2. Slight impurities in the *d*-glucose are apt strongly to color the reaction mixture but do not materially affect the yield.

3. The final mother liquor, on long standing, deposits a further crop (about 6 g.) of crystals which melt at 94–96° and consist largely of β-methyl glucoside. A further quantity of the α-glucoside may be obtained by distilling all the ethyl alcohol and boiling the residue with methyl alcoholic hydrogen chloride; it is questionable, however, whether the yield repays the time spent on the operation.

## 3. Other Methods of Preparation

The above procedure is based on that of Emil Fischer.[1] It differs, however, in the important detail that the use of an autoclave or pressure bottle is avoided,—a simplification due to Bourquelot.[2] The biochemical synthesis of Bourquelot has been developed to a preparative method by Aubry,[3] but it is less convenient and gives poorer yields.

[1] Ber. **28**, 1151 (1895).

[2] Ann. chim. (9) **3**, 298 (1915). *Cf.* Zemplen and Tulok; Aberhalden, *Biochemisches Handlexikon* **10**, 770 (1923). Unpublished observation.

[3] J. pharm. chim. (7) **10**, 202 (1914).

# MYRISTIC ACID

$$CH_2(OCOC_{13}H_{27})CH(OCOC_{13}H_{27})CH_2(OCOC_{13}H_{27})+3NaOH \rightarrow 3C_{13}H_{27}CO_2Na+CH_2OHCHOHCH_2OH$$

$$C_{13}H_{27}CO_2Na+HCl \rightarrow C_{13}H_{27}CO_2H+NaCl$$

Submitted by G. D. BEAL.
Checked by H. T. CLARKE and E. R. TAYLOR.

## 1. Procedure

IN a 2-l. round-bottom flask are placed 100 g. (0.14 mole) of pure (Note 1) trimyristin (p. 100) and 200 cc. of 10 per cent sodium hydroxide solution. The mixture is heated on a steam bath for two hours, with frequent shaking or stirring until the trimyristin has become emulsified. It is then diluted with 300 cc. of water and the heating is continued for another half hour, by which time the solution should be almost clear, indicating complete saponification. The solution is now poured with stirring into a hot solution of 650 cc. of water and 100 cc. of 20 per cent hydrochloric acid. The free acid which separates is not entirely clear, owing to the presence of unchanged sodium salt (Note 2). A gentle current of steam is passed into the hot mixture until the oily layer is transparent; this requires about fifteen minutes. The acid is allowed to cool and solidify; it is removed and freed of small quantities of salt and water by filtering through paper in a steam-jacketed funnel. The yield is 84–90 g. (89–95 per cent of the theoretical amount) of a colorless product (Note 3) which melts at 52–53° (Note 4).

## 2. Notes

1. If the trimyristin is not pure white and free of nutmeg oil, it will be necessary to purify the resulting acid by distillation

under reduced pressure. It boils at 250°/100 mm. and 195°/15 mm.

2. As much as 15–20 g. of sodium salt may be found in the acid at this point if care be not taken to insure its decomposition. A corresponding amount of 35 per cent hydrochloric acid may be used. An excess of acid does no harm.

3. If desired, the acid may be recrystallized from petroleum ether (b.p., 40–60°) (F. H. Carr, private communication).

4. The melting point is not appreciably raised by recrystallization from petroleum ether. The highest melting point recorded in the literature is 53.8°.

## 3. Other Methods of Preparation

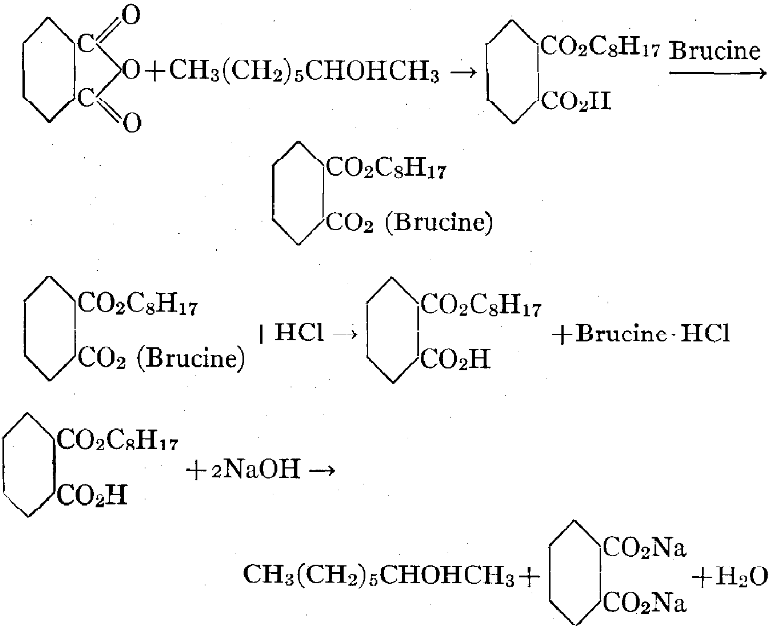
Myristic acid occurs as a glyceride in many vegetable fats and oils, in particular in coconut oil,[1] its isolation from which involves separation from homologs by fractional distillation of the acids or their esters. The trimyristin obtained from nutmegs[2] (p. 100) or from the seeds of *Virola venezuelensis*[3] forms the most suitable source.

[1] Ann. **66**, 314 (1848).
[2] Ber. **12**, 1668 (1879).
[3] Ber. pharm. Ges. **11**, 263 (1901) (Chem. Zentr. **1901, II,** 189).

# XXI

## *d*- and *l*-OCTANOL-2

(Optically Active *Sec*.-Octyl Alcohols)



Submitted by JOSEPH KENYON.
Checked by ROGER ADAMS and F. E. KENDALL.

### 1. Procedure

A. *Preparation of Sec.-Octyl Hydrogen Phthalate.*—A mixture of 130 g. (1 mole) of *sec*.-octyl alcohol (Org. Syn. **1**, 61) and 148 g. (1 mole) of phthalic anhydride is heated for twelve to fifteen hours in a flask surrounded by an oil bath at 110–115° (Note 1). During the heating the mixture should be mechanically stirred

or shaken occasionally to give a homogeneous liquid. The cooled reaction mixture is added to about 8 l. of water which contains 150 g. (1.5 moles) of anhydrous sodium carbonate. The solid material gradually goes into solution, and if the resulting solution is perfectly clear, dilute hydrochloric acid is added in slight excess, thus precipitating the *sec.*-octyl hydrogen phthalate as an oil which rapidly turns to a solid; if the alkaline solution is not clear owing to the presence of methyl hexyl ketone in the original alcohol, it should be extracted with ether to remove the ketone before acidifying with hydrochloric acid.

The octyl hydrogen phthalate is filtered, washed with water, ground thoroughly with water in a mortar and finally filtered and dried. For complete purification it may be crystallized either from petroleum ether (b.p. 60–70°) or glacial acetic acid from which it separates as needles melting at 55°. The crude material, however, is perfectly satisfactory for the following experiments. The yield is nearly quantitative if the *sec.*-octyl alcohol is pure (Note 2).

B. *Resolution.*—A warm solution of 278 g. (1 mole) of *sec.*-octyl hydrogen phthalate and 600 cc. of acetone is treated with 394 g. (1 mole) of brucine and the mixture warmed until the solution is clear. Upon cooling, the crystals of brucine salt (A) form. These are filtered, pressed and washed in the funnel with 250 cc. of acetone. The combined filtrate and washings are concentrated to about 50 per cent of their original volume and then poured into dilute hydrochloric acid (slightly more than the calculated amount) which causes the precipitation of the *sec.*-octyl hydrogen phthalate. After it sets to a crystalline mass, it is filtered, washed with cold water and dried. This weighs approximately one-half of the original ester used and has a rotation $(\alpha)_{5461} -47°$ in absolute alcohol solution (Note 3).

The crystals (A) are dissolved in a minimum amount of hot ethyl alcohol and decomposed by pouring the solution into dilute hydrochloric acid. The weight of the ester thus obtained is about half of that originally taken and its rotation in absolute alcohol is about $(\alpha)_{5461}+47°$, $(\alpha)_D+44°$.

The two lots of crude active *sec.*-octyl hydrogen phthalates

are now separately crystallized twice from acetic acid (about twice its weight of 90 per cent acetic acid should be used for solution in each case). They are thus obtained in an optically pure condition and possess the rotations $(\alpha)_{5461}$ $-58.5°$, $(\alpha)_D -48.4°$ and $(\alpha)_{5461} +58.3°$, $(\alpha)_D +48.4°$, respectively. The amount of pure product, m.p. 75°, obtained in each case is respectively about 99 g. and 96 g. (about 70 per cent of the theoretical amount). The *sec.*-octyl hydrogen phthalate of low optical activity obtained by adding water to the acetic acid filtrates can be collected and used in a subsequent preparation.

Optically pure *l*- and *d-sec.*-octyl alcohols are obtained by distillation in a current of steam of the *sec.* octyl hydrogen phthalate and 2 moles of sodium hydroxide in 30 per cent solution. The alcohols are practically insoluble in water and are separated, dried with potassium carbonate and distilled. Each boils at 86°/20 mm. and has a rotation $(\alpha)_{5461}^{17°} +11.8°$, $(\alpha)_D^{17°} +9.9°$ or $(\alpha)_{5461}^{17°} -11.8°$, $(\alpha)_D^{17°} -9.9°$. The yields of alcohol from the *sec.*-octyl hydrogen phthalates are about 95 per cent of the calculated amounts.

## 2. Notes

1. If this temperature is exceeded the yield of octyl phthalate is reduced and the color of the product is very dark. The color is carried through with the *l*-fraction, making it difficult to read rotations.

2. The yield of *sec.*-octyl hydrogen phthalate from the crude *sec.*-octyl alcohol used in this preparation was 61–64 per cent.

3. This product is frequently so dark that a determination of rotation is impossible.

## 3. Other Methods of Preparation

The resolution of *sec.*-octyl alcohol was first described by Pickard and Kenyon.[1] The method employed by these authors differed from the foregoing in the following respects. The brucine salt of *sec.*-octyl hydrogen phthalate was crystallized several times from acetone until it reached optical purity and was then decom-

posed to give pure *d-sec.*-octyl hydrogen phthalate. The partly laevo-rotatory hydrogen phthalic ester obtained by the decomposition of the more soluble fractions of the brucine salt was then combined with cinchonidine and the cinchonidine salt crystallized some half dozen times from acetone until optical purity was reached. Decomposition of this salt yielded the optically pure *l-sec.*-octyl hydrogen phthalate.

The second and much more convenient procedure given above was described by Kenyon.[2]

[1] J. Chem. Soc. **91**, 2058 (1907).
[2] J. Chem. Soc. **121**, 2540 (1922).

# XXII

## PHENYL ISOTHIOCYANATE

$$C_6H_5NH_2 + CS_2 + NH_4OH \rightarrow C_6H_5NHCS_2NH_4 + H_2O$$

$$C_6H_5NHCS_2NH_4 + Pb(NO_3)_2 \rightarrow C_6H_5NCS + NH_4NO_3 + HNO_3 + PbS$$

Submitted by F. B. DAINS, R. Q. BREWSTER and C. P. OLANDER.
Checked by C. S. MARVEL and L. T. SANDBORN.

### 1. Procedure

IN a 500-cc. round-bottom flask (Note 1) fitted with a mechanical stirrer and surrounded by an ice-salt cooling bath, are placed 54 g. (0.71 mole) of carbon disulfide and 90 cc. (1.3 moles) of concentrated ammonium hydroxide (sp. g. 0.9). The stirrer is started and 56 g. (0.6 mole) of aniline (Note 2) is run into the mixture from a separatory funnel at such a rate that the addition is complete in about twenty minutes. The stirring is continued for thirty minutes after all of the aniline has been added, and then the reaction mixture is allowed to stand for another thirty minutes. During this time a heavy precipitate of ammonium phenyl dithiocarbamate separates and may even stop the stirrer.

The salt is dissolved in 800 cc. of water (Note 3) and transferred to a 5-l. round-bottom flask. To the solution is added with constant stirring a solution of 200 g. of lead nitrate (0.6 mole) in 400 cc. of water. Lead sulfide separates as a heavy brown precipitate which soon turns black. The mixture is then distilled with steam into a receiver containing 5–10 cc. of 1 N sulfuric acid as long as any oil comes over (Note 4). About 2–3 l. of distillate is collected. The product is separated from the water and weighs 63–66 g.

The oil is dried over a little calcium chloride and distilled under reduced pressure. The yield of phenyl isothiocyanate

boiling at 120–121°/35 mm. is 60–63 g. (74–78 per cent of the theoretical amount) (Notes 5 and 6).

## 2. Notes

1. If the reaction is carried out in a beaker, so much ammonia is lost by volatilization that the crystalline ammonium phenyl dithiocarbamate is not formed. The temperature should be from 0–10° to avoid loss of ammonia.

2. Ordinary technical aniline was used in these experiments.

3. The transfer of the salt to the 5-l. flask is conveniently made by the addition of four successive 200-cc. portions of water to the flask containing the salt.

4. The sulfuric acid is added to react with any ammonia that may be carried over. Otherwise the ammonia may react with the product to give mono- and diphenylthiourea.

5. Larger runs give somewhat lower percentage yields; thus 280 g. of aniline gives about 250 g. (60 per cent of the theoretical amount) of redistilled phenyl isothiocyanate.

6. This reaction is a general method of preparation for aryl isothiocyanates in yields of 50–75 per cent of the theoretical amount.

## 3. Other Methods of Preparation

Phenyl isothiocyanate has been prepared from thiocarbanilide by the action of phosphorus pentoxide,[1] hydrochloric acid,[2] iodine,[3] phosphoric acid,[4] acetic anhydride,[5] and nitrous acid.[6] It has also been prepared from ammonium phenyl dithiocarbamate by the action of ethyl chlorocarbonate,[7] copper sulfate [8, 10], lead carbonate,[9] lead nitrate,[10] ferrous sulfate,[10] and zinc sulfate.[10]

[1] Jahresber. **1858**, 349.

[2] Z. Chem. **1869**, 589.

[3] Ber. **2**, 453 (1869); J. Russ. Phys. Chem. Soc. **10**, 184 (1878).

[4] Ber. **15**, 985 (1882).

[5] J. Chem. Soc. **59**, 396 (1891).

[6] Monatsh. **27**, 277 (1906).

[7] Monatsh. **33**, 367 (1912).

[8] Ber. **24**, 3021 (1891).

[9] J. prakt. Chem. (2) **65**, 366 (1902).

[10] Univ. Kansas Sci. Bull. **13**, 1 (1922).

## XXIII

# 4-PHENYLSEMICARBAZIDE

$$C_6H_5NHCONH_2+NH_2NH_2\cdot H_2O \rightarrow C_6H_5NHCONHNH_2+NH_3+H_2O$$

Submitted by A. S. Wheeler.
Checked by C. S. Marvel and M. M. Brubaker.

## 1. Procedure

In a 500-cc. round-bottom flask fitted with a reflux condenser are placed 68 g. of phenylurea (0.5 mole) (Note 1) and 120 cc. (1 mole) of 42 per cent hydrazine hydrate solution (Note 2). The flask is heated on a steam bath for about twelve hours. The hot mixture is treated with a small amount of decolorizing charcoal (Norite) and filtered. The charcoal is washed with two 15-cc. portions of warm water and the filtrate and washings are then concentrated on a steam bath to about 100 cc. On cooling in an ice bath a crop of crystals separates and is collected on a filter and washed with two 15-cc. portions of cold water. The filtrate and washings are concentrated to about 25 cc. and another crop of crystals is obtained as before. The total yield of crude compound is 47–52 g. It is white at first but sometimes turns brown on drying. It usually melts below 115° because of some unchanged phenylurea.

The product is purified (Note 3) by conversion to the hydrochloride which is then changed into the free base.

A filtered solution of the crude product in 200 cc. of hot absolute alcohol is treated with 250 cc. of concentrated hydrochloric acid. Most of the hydrochloride precipitates at once and is filtered, washed with alcohol and dried. The filtrate is cooled in an ice-salt bath and again filtered, and the precipitate is

washed, dried and added to the previous portion. The yield is 46–48 g. of material melting at about 215° (Note 4). The hydrochloride is dissolved in three times its weight of water, previously heated nearly to boiling (Note 5). The solution is filtered if necessary and then treated with sodium hydroxide solution (2.2 g. of 10 per cent sodium hydroxide solution for each gram of hydrochloride used). The free base separates at once and the solution is cooled in an ice bath and filtered. This product melts at 120–123°. The yield of pure base is 28–30 g. (37–40 per cent of the theoretical amount).

## 2. Notes

1. The phenylurea was prepared as described in Org. Syn. **3,** 95 and melted at 146–147°.

2. An equivalent amount of hydrazine sulfate and sodium hydroxide in 80 per cent alcohol may be used in place of the hydrazine hydrate solution without greatly diminishing the yield.

3. The crude product contains about 9–10 g. of unchanged phenylurea which cannot be satisfactorily removed by crystallization from benzene or water. When the hydrochloride of the phenylsemicarbazide is formed, the phenylurea may be recovered from the alcoholic filtrates.

4. Inasmuch as the melting point of the salt varies somewhat with the rate of heating, this temperature is not particularly significant.

5. The salt should not be boiled with water any longer than is necessary, as some decomposition occurs and diphenylurea, melting at about 235–240°, is produced.

## 3. Other Methods of Preparation

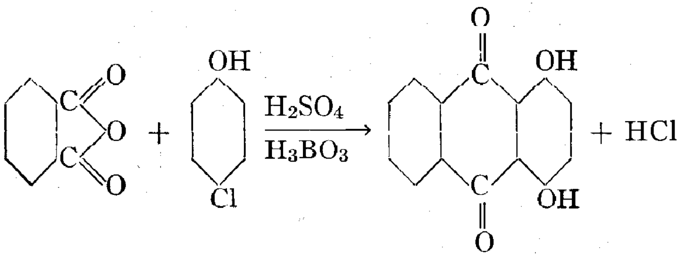
4-Phenylsemicarbazide has been obtained by the action of hydrazine hydrate on diphenylurea,[1] phenylurethane,[1] phenyl isocyanate,[1] or the potassium salt of dibenzohydroxamic acid.[2] For its preparation, Curtius' method of treating phenylurea with hydrazine hydrate[1] is better than either the older method of

treating acetyl phenylsemicarbazide with sulfuric acid and benzaldehyde and subsequent hydrolysis of the benzal 4-phenylsemicarbazone[3] or the more recent method which involves the hydrolysis of $\alpha$-benzoyl $\beta$-phenylcarbamyl hydrazine.[4]

[1] J. prakt. Chem. (2) **58**, 216 (1898).
[2] Ann. **309**, 193 (1899).
[3] J. prakt. Chem. (2) **53**, 526 (1896).
[4] J. Am. Chem. Soc. **39**, 1333 (1917).

XXIV

## QUINIZARIN



Submitted by L. A. BIGELOW and H. H. REYNOLDS.
Checked by ROGER ADAMS and G. S. HIERS.

### 1. Procedure

ONE hundred fifteen grams (0.9 mole) of *p*-chlorophenol, 300 g. (2.0 moles) of phthalic anhydride, 50 g. of crystallized boric acid and 2000 g. of 95 per cent sulfuric acid are thoroughly mixed in a 1.5-l. round-bottom flask. The flask is then immersed to the neck in an oil bath and the temperature gradually raised to 200° during the course of one-half to three-quarters of an hour (Note 1). It is then kept constant at 200° for three and one-half hours. Owing to the tendency of the phthalic anhydride to sublime, the mouth of the flask is covered with a piece of porous plate. When cool, the colored melt is poured slowly into 5 l. of cold water with continuous stirring, and filtered. The precipitate is boiled with 10 l. of water and filtered hot to remove the excess of phthalic anhydride which goes into solution. The residue is then suspended in 10 l. of boiling water and to this suspension is added a sufficient quantity of 10 N potassium hydroxide solution to produce a purple color (about 30 cc.), followed by 300 cc. more (Note 2). The alkaline solution is filtered hot, and the resi-

due (about 5–10 g.) washed with 200 cc. of hot 2 per cent potassium hydroxide solution and discarded.

The purple quinizarin solution is next saturated with carbon dioxide and the precipitated quinizarin again filtered. The product is then boiled with 5 l. of a 10 per cent solution of sodium carbonate until it appears black (probably the mono-sodium salt) to dissolve the last traces of purpurin. The mixture is cooled to room temperature, filtered, and the precipitate boiled with 5 l. of 5 per cent hydrochloric acid to liberate the quinizarin. The mixture is again cooled to room temperature and the final product filtered, washed with cold water and dried at 100°.

The yield is 147–160 g. (68–74 per cent of the theoretical amount). It sinters at 190–191° and melts at 199–200° (corr.). A sample twice recrystallized from glacial acetic acid melted at 200–202° (corr.) (Note 3). The crystal form of this product compares very favorably with that of quinizarin of the highest purity, as observed under the microscope.

## 2. Notes

1. An enameled bucket placed on a Fletcher radial burner serves well for this purpose.

2. The "purple color" end point is not sharp, but as soon as the red hue of the mixture has distinctly changed toward purple, this point is considered reached. A variation of 5–10 cc. either way has little effect, but a large excess gives a large alkali-insoluble residue.

3. Purified quinizarin is reported as melting at 194–195° (*Ber.* **6**, 508 (1873). A melting point of 191–193°, probably uncorrected, is also given (*Ann.* **212**, 13 (1882)).

## 3. Other Methods of Preparation

Quinizarin has been prepared by heating *p*-chlorophenol, phthalic anhydride, and sulfuric acid;[1] by heating hydroquinone with phthalic anhydride;[2] by heating hydroquinone, phthalic anhydride and C.P. sulfuric acid;[3] by oxidizing anthraquinone

with ammonium persulfate in sulfuric acid solution;[4] by treating anthraquinone and 2-hydroxyanthraquinone with sulfuric and nitric acids in the presence of boric acid;[5] by heating anthraquinone with sulfuric acid in the presence of boric acid to 260–280°;[6] and by chlorination of hydroxy-anthraquinone followed by hydrolysis with sulfuric acid in the presence of boric acid.[7]

[1] Ber. **8**, 152 (1875).
[2] Ber. **6**, 506 (1873).
[3] Ann. **212**, 11 (1882).
[4] J. prakt. Chem. (2) **54**, 90 (1896).
[5] Ger. pat. 81,245, 86,630; Frdl. **4**, 296, 301 (1894–97).
[6] Ger. pat. 81,960; Frdl. **4**, 274 (1894–97).
[7] U. S. pat. 1,504,165 (C. A. **1925**, 77).

XXV

# *dl*-TARTARIC ACID

(By-product, Meso-Tartaric Acid)

$$\begin{array}{l} CHOHCO_2H \\ | \qquad\qquad\qquad \cdot H_2O \\ CHOHCO_2H \end{array}$$

Submitted by A. F. HOLLEMAN.
Checked by H. T. CLARKE and H. J. BEAN.

## 1. Procedure

IN a copper or iron kettle of 4-l. capacity is placed a solution of 200 g. of *d*-tartaric acid and 700 g. of sodium hydroxide in 1400 cc. of water. A 12-l. flask through which cold water is run is placed in the mouth of the kettle in order to prevent loss of water vapor, and the mixture is boiled gently over an open flame for four hours. The solution is now transferred to a 12-l. flask or crock and partially neutralized with 1400 cc. of commercial hydrochloric acid (density 1.19). To the still alkaline solution is now added just enough sodium sulfide to precipitate all the iron or copper which has been dissolved from the kettle (Note 1). The filtered solution is then just acidified with hydrochloric acid, boiled to expel all hydrogen sulfide, and made very faintly alkaline to phenolphthalein with sodium hydroxide solution. To the hot solution is then added a concentrated solution of 300 g. of anhydrous calcium chloride which causes an immediate precipitation of calcium *dl*-tartrate and mesotartrate.

The mixture is allowed to stand for a week (Note 2) and the precipitate filtered, washed with cold water until free of chlorides, and dried at 40–50°. The yield is 246–315 g. The product

is found on analysis to consist principally of the tetrahydrate, $C_4H_4O_6Ca \cdot 4H_2O$, (Note 3). It is suspended in 800 cc. of water and treated with the calculated quantity (0.4 g. for every 1.0 g.) of concentrated (95–96 per cent) sulfuric acid. The mixture is warmed on the steam bath, with occasional shaking, or mechanical stirring, for thirty to forty hours (Note 4), filtered hot, and the calcium sulfate washed well with hot distilled water.

The united filtrate is evaporated on the steam bath until the volume amounts to 200 cc., at which point crystals should have already begun to separate from the hot solution. After standing at room temperature for twenty-four hours or longer, the crystals are filtered by suction as free from mother liquor as possible and recrystallized from an equal weight of distilled water (Note 5). The filtrate from this recrystallization is evaporated on the steam bath and the second crop of *dl*-tartaric acid filtered and recrystallized as before. The yield is 65–75 g. (32.5–35.5 per cent of the theoretical amount).

The sirupy filtrate from the *dl*-tartaric acid, which consists principally of meso-tartaric acid together with a small amount of unchanged *d*-tartaric acid, is diluted with its own volume of water and divided into two equal parts; one part is exactly neutralized with potassium hydroxide, using phenolphthalein, and the second part is added. After standing for twenty-four hours the potassium hydrogen *d*-tartrate is filtered off. The filtrate is neutralized with ammonia, then just acidified with acetic acid, and treated with an excess of calcium chloride solution (about 500 cc. of a 25 per cent solution). After standing for a week (Note 2) the precipitated calcium meso-tartrate is filtered and washed with cold distilled water. It may, if desired, be recrystallized from boiling water. The yield is 42–55 g. (corresponding to 14–18 per cent of the original *d*-tartaric acid). The sirupy free acid may be prepared from this salt by treatment with sulfuric acid as above.

## 2. Notes

1. If iron is not removed at this point it separates with the calcium salt and contaminates the final product. If desired,

copper can be removed at a later stage by passing hydrogen sulfide through the acid solution.

2. The calcium salts, in particular that of meso-tartaric acid, separate very slowly, and the yield is appreciably lower if the mixture is allowed to stand only eighteen hours.

3. The calcium salt of the principal product, *dl*-tartaric acid, crystallizes with four molecules of water, while the secondary product, meso-tartaric acid, forms a calcium salt which crystallizes with three molecules of water. The amount of sulfuric acid actually required may readily be calculated from the percentage of calcium found on analysis in the regular way; or it may be estimated by igniting a sample, and titrating the residue with standard acid.

4. This long treatment is necessary since, on the one hand, the calcium salts tend to be protected by the calcium sulfate which crystallizes on them, and on the other hand, it is important to allow all the free sulfuric acid to react.

5. A very complete separation of the calcium sulfate may be effected by adding to the concentrated solution 1000 cc. of alcohol, allowing the mixture to stand for 24 hours, and filtering. The alcohol is then distilled from the filtrate and the procedure followed as indicated above.

### 3. Other Methods of Preparation

The most practical method for preparing *dl*-tartaric acid consists in the racemization of *d*-tartaric acid. This was first accomplished by Pasteur [1] by heating cinchonine *d*-tartrate; it can also be brought about (though with poor yield) by boiling with dilute mineral acids,[2] or with water,[3] or by heating the acid to 170–180°.[3] A better yield is obtained by heating *d*-tartaric acid to 175° with a small amount of water,[4] or by boiling with a large excess of concentrated alkali.[5]

*dl*-Tartaric acid has been produced synthetically by a variety of methods, the most interesting of which is the oxidation of fumaric acid; [6] maleic acid on oxidation yields meso-tartaric

acid [7] which is always formed as a by-product during the racemization of tartaric acid.

[1] Jahresber. **1853**, 422.
[2] Jahresber. **1856**, 463; Rec. trav. chim. **17**, 65 (1898).
[3] Bull. soc. chim. **5**, 355 (1863).
[4] Compt. rend. **75**, 439 (1872); Bull. soc. chim. (2) **18**, 201 (1872).
[5] Ber. **30**, 1574 (1897); Rec. trav. chim. **17**, 65 (1898).
[6] Ber. **13**, 2150 (1880); **46**, 1667 (1913); J. Am. Chem. Soc. **47**, 1412 (1925).
[7] Ber. **14**, 713 (1881); **46**, 1667 (1913); J. Am. Chem. Soc. **47**, 1412 (1925).

# XXVI

## THIOPHOSGENE

$$2CS_2 + 5Cl_2 \rightarrow 2CSCl_4 + S_2Cl_2$$

$$2S_2Cl_2 + 2H_2O \rightarrow SO_2 + 3S + 4HCl$$

$$CSCl_4 + 2H \rightarrow CSCl_2 + 2HCl$$

Submitted by G. Malcolm Dyson.
Checked by Frank C. Whitmore and A. M. Griswold.

### 1. Procedure

A. *Preparation of Thiocarbonyl Perchloride.*—In a 5-l. bottle arranged for cooling by running water is placed 500 g. (6.58 moles) of dry carbon disulfide (Note 1) to which 0.5 g. of iodine has been added. Dry chlorine is passed into the cooled carbon disulfide at such a rate that the temperature does not rise above 25°, until the liquid weighs 1770 g. (17.9 moles chlorine) (Note 2). The time required is about forty hours. The product is a deep red liquid, a mixture of impure thiocarbonyl perchloride and sulfur chloride.

The apparatus illustrated in Fig. 3 is assembled, in a large hood if possible (Note 3). *A* is a 5-l. round-bottom flask heated by a large ring burner and provided with a specially treated four-hole cork stopper covered with tin foil (Note 4). To these holes are fitted the column *D*, the tube *B* reaching to the bottom of *A*, the specially bent tube *C* reaching up the inside of *D*, and the tube *K* connected with the tubes leading to the 2-l. separatory funnel *H*, so that the distance between the stopper of *A* and the stopcock of *H* is at least 100 cm. The bottom of the column *D* is of 20 mm. bore while the main portion is 30 mm. The side arm should be at least 85 cm. above the stopper of *A*. The tube *C*

should reach about half way up the inside of the column *D*. The column is filled with pieces of 3-mm. glass tubing about 5 mm. long. Its top is provided with a cork covered with tin foil and fitted fairly loosely so as to blow out in case of a clogging of the apparatus. It should be held by a wire to prevent its being blown out entirely. Tubes *B* and *C* are connected with a steam line or steam generator of large capacity. The separatory funnel

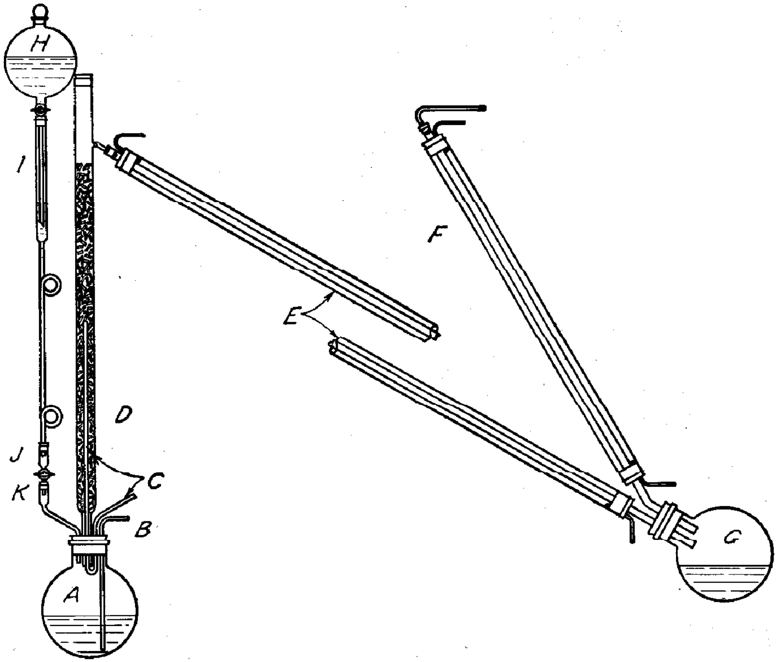



FIG. 3.

*H* is placed at the highest available level (Note 5) and connected with the tubes *I*, *J*, and *K* in such a manner as to secure a pressure of liquid sufficient to more than balance the steam pressure (Note 6). *E* and *F* are specially constructed condensers of unusual length (160 cm. and 85 cm., respectively) and bore (40 mm.) made from large glass tubing and rubber stoppers (Note 7). The top of condenser *F* is connected to a good draft chamber.

*G* is a 5-l. or better, a 12-l. round-bottom flask which is used as a receiver.

The crude chlorinated mixture is steam-distilled in the special apparatus to obtain thiocarbonyl perchloride and to decompose the sulfur chloride. In flask *A* is placed 1200 cc. of water which is heated to boiling by means of the ring burner. Steam is passed in through tubes *B* and *C*. The chlorinated mixture is placed in the separatory funnel *H* and the connecting tubes are filled with the liquid which is allowed to pass into *A* at about 5 drops per second (Note 8). Sulfur begins to separate in the column and in the condensers. The steam distillation requires about five hours and gives 10–12 l. of distillate consisting of water, sulfur and a heavy red oil. The water is decanted and the rest of the mixture is filtered by suction through glass wool. The oil is separated and dried over about 10 g. of calcium chloride.

The crude, dry thiocarbonyl perchloride is distilled through an efficient 60-cm. column (Note 9). The distillate below 140° is discarded. The fraction boiling at 140–155° at atmospheric pressure amounts to about 600 g. The boiling point of pure thiocarbonyl perchloride is 149°.

B. *Reduction of Thiocarbonyl Perchloride to Thiophosgene.*— The apparatus illustrated in Fig. 4 is assembled. A is a 5-l. round-bottom flask heated by a ring burner and provided with a two-hole, specially treated cork (Note 4) carrying tube *B* of about 40 cm. length connected with condenser *C* of about 115 cm. length, and tube *R* which conveys the perchloride from the separatory funnel *T* (Note 6). *R* is 6 mm. tubing of about 90 cm. length and must reach to the bottom of *A*. *D* and *G* are specially blown connecting tubes, *D* reaching through the cork of *F* and *G* reaching to the bottom of the 5-l. flask, *F*. Each arm of *D* is about 20 cm. long and 2 cm. bore. The vertical arm of *G* is of about 3 cm. bore and its side arm of about 1 cm. bore. *H* and *I* are efficient bulb condensers at least 60 cm. long. *F* is provided with siphon *E* for removing the product. *L* is a tall calcium chloride tower (about 50 cm. in length) packed with short pieces of glass tubing with layers of glass wool. Its stopper carries the tube *K* reaching to the bottom of the tower, a

separatory funnel, and an exit tube *M* leading to the draft. *P* is a siphon for removing the xylene wash liquid.

In the flask *A* are placed 750 g. (6.3 moles) of granulated tin (Note 10) and 1500 cc. of commercial hydrochloric acid (about 28 per cent). The mixture is heated until the action is vigorous. The thiocarbonyl perchloride is run in from the funnel *T* (Note 11). The resulting reaction is very violent. The vapors are

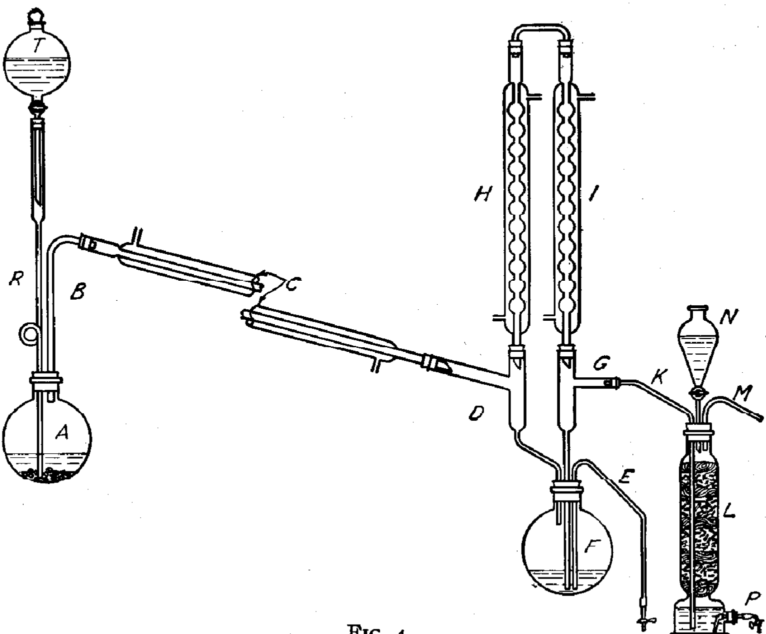



FIG. 4.

condensed in the series of condensers and in the scrubber *L* through which xylene is allowed to flow slowly from the separatory funnel *N*. Most of the crude thiophosgene collects in *F*, although a small amount is obtained from the distillation of the xylene wash liquid.

The crude thiophosgene is separated and dried with about 10 g. of calcium chloride, and fractionated with a good column. Very little distils below 73°. The fraction boiling at 73–76° at atmospheric pressure is pure thiophosgene and amounts to about

180 g. (24 per cent of the theoretical amount) (Note 12). The fraction above 76° is unchanged thiocarbonyl perchloride and may be again reduced or added to the reduction in a subsequent run.

## 2. Notes

1. Ordinary commercial carbon disulfide was used after drying over calcium chloride.

2. Any great excess of chlorine should be avoided as it favors the formation of carbon tetrachloride. Practically as good yields have been obtained by using only about three-quarters the amount of chlorine indicated.

3. The vapors formed in the experiment are very objectionable. It is even advisable to transfer the liquids from one vessel to another by suction rather than by pouring in order to avoid the irritating and lachrymatory effects of the vapors.

4. It is advisable to saturate all corks with sodium silicate solution after fitting and boring them (p. 3, Note 1). They are then covered with lead foil, wired in, and coated with shellac.

5. As long a column of liquid as possible is used to overcome the tendency for steam to work back up the inlet tube. If this happens, the sulfur formed is likely to clog the tube. This can be avoided by proper manipulation of the stopcock *J*.

6. The backing of steam up the inlet tube is one of the most serious difficulties in the experiment. This can be avoided if the tube *I* (Fig. 3) is once filled with the perchloride.

7. No ordinary condenser was found sufficiently effective to condense the vapors and not be clogged by the sulfur. The *specially constructed wide condensers are absolutely necessary.*

8. If the addition is much more rapid than this, the sulfur chloride is not all decomposed.

9. The distillation of the crude perchloride is necessary to remove carbon tetrachloride and other low-boiling impurities which could not later be separated from the thiophosgene by distillation.

10. The tin used should be in fairly large granules, otherwise the reaction is likely to become too violent. In general, the

faster the reduction the better the yield of thiophosgene. In a few cases yields of 50–60 per cent have been obtained.

11. The time of addition of the perchloride should be made as short as possible consistent with safety. In runs with the above amounts of materials, the time of the addition was about ten minutes. It may again be emphasized that the yield depends largely on the skill of the operator in running the reduction as rapidly as possible.

12. As has been stated, larger yields are occasionally obtained but they cannot be depended on.

### 3. Other Methods of Preparation

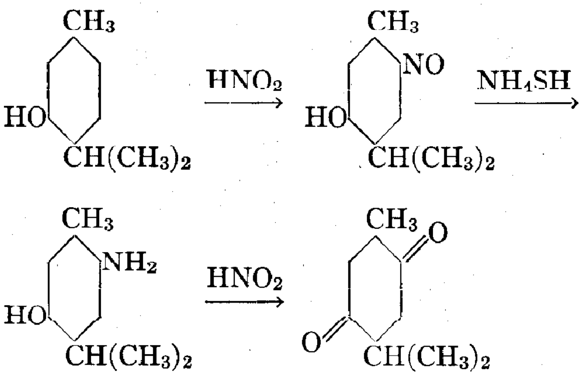
Thiophosgene has been prepared in small yield by the chlorination of carbon disulfide in the presence of iodine [1] and by the reduction of thiocarbonyl perchloride.[2]

[1] Ber. **3**, 858 (1870).

[2] Ber. **20**, 2376 (1887); J. Am. Chem. Soc. **38**, 1551 (1916); J. Soc. Chem. Ind. **39**, 256 (1920). Gazz. chim. ital. **53**, 175 (1923); **54**, 251 (1924).

XXVII

# THYMOQUINONE



Submitted by EDWARD KREMERS, NELLIE WAKEMAN and R. M. HIXON.
Checked by H. T. CLARKE and C. R. NOLLER.

## 1. Procedure

A. *Nitrosothymol.*—To a solution of 100 g. (0.666 mole) of thymol in 500 cc. of 95 per cent ethyl alcohol is added 500 cc. of concentrated hydrochloric acid. This mixture is cooled to 0° in a 2-l. beaker set in an ice-salt bath, and to it is added 72 g. (1 mole) of commercial sodium nitrite in portions of about 5 g. each.

The mixture is stirred well after each addition (Note 1). The solution first becomes brown in color, and a green precipitate soon begins to form. After 35 g. of nitrite has been added, the mixture becomes pasty; the intervals between the additions must now be lengthened and the stirring made more vigorous. When all has been added, the bulk of the product is transferred to

a 12-l. flask containing 8 l. of cold water, and the remainder washed in with water. The product, after agitation with water, is now a light-yellow, fluffy solid; it is filtered off by suction and washed well with water (Note 2).

B. *Aminothymol.*—The crude, wet nitrosothymol so obtained is worked up with a mixture of 900 cc. of 28 per cent ammonia water (sp. g. 0.90) and 1600 cc. of water; the brown solution is filtered free of a little resinous matter, and hydrogen sulfide is passed into it. The brown color disappears and a white precipitate of aminothymol forms. The passage of hydrogen sulfide is continued for thirty minutes longer (Note 3), when the base is filtered and washed well with cold water, contact with air being avoided as far as possible (Note 4).

C. *Thymoquinone.*—The wet aminothymol thus prepared is immediately dissolved in 110 cc. of concentrated sulfuric acid diluted to 4 l. and contained in a 12-l. flask. To this solution is added 150 g. of sodium nitrite (2.18 moles), in 5–10-g. portions, with shaking after each addition. The resulting mixture is heated to 60° on a steam bath, with occasional shaking, for half an hour (Note 5), and is then distilled in a current of steam, by means of the apparatus described in Org. Syn. **2**, 80 (Note 6). All the thymoquinone passes over with the first 3 l. of distillate; it solidifies on cooling, and is filtered with suction (Note 7), washed, and dried at room temperature. The yield is 80–87 g. (73–80 per cent of the theoretical amount) of bright yellow crystals, melting at 43–45° (Note 8).

## 2. Notes

1. No nitrous acid escapes from the mixture, since it is converted into ethyl nitrite which in turn reacts with the thymol.

2. The crude nitrosothymol may be purified by drying and subsequent recrystallization from 2 l. of benzene, from which it separates as a pale yellow solid, melting at 160–164°. A small second crop is obtained on concentrating the mother liquor,

which contains in addition an orange-colored resinous impurity. The yield is 103 g. (87 per cent of the theoretical amount).

3. If the base is filtered off without passing in the excess of hydrogen sulfide, it immediately assumes a purple color on exposure to air.

4. The free base tends to become oxidized in the air but may be preserved as the hydrochloride. This is prepared by transferring it as soon as possible to 1500 cc. of distilled water containing 100 cc. of concentrated hydrochloric acid. The sparingly soluble hydrochloride separates at once. It is recrystallized from the mixture with the use of a little decolorizing carbon, whereupon it separates as colorless needles. A further crop is obtained on concentrating the mother liquor under reduced pressure to about 200 cc. The yield is 110 g. (82.1 per cent of the theoretical amount).

5. The greater part of the oxides of nitrogen escapes during this treatment; the small amount that passes over with the thymoquinone does not harm the product.

6. If an ordinary condenser is employed for the steam distillation, care must be taken that the distilled product does not crystallize in the condenser tube and clog it.

7. The watery filtrate contains about 0.5 g. of dissolved thymoquinone; this can be recovered by distilling over 500 cc. of it and filtering the distillate.

8. The melting point is not appreciably raised by recrystallization from petroleum ether (b.p. 60–80°).

## 3. Other Methods of Preparation

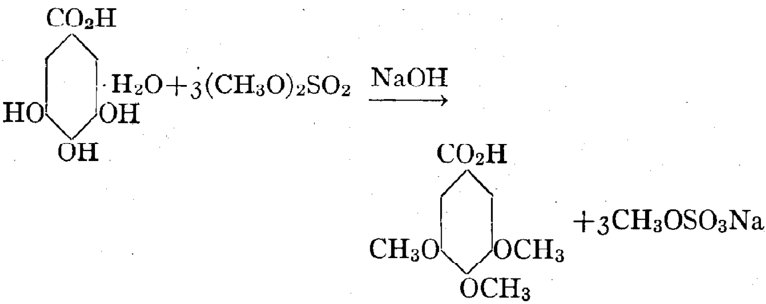
Thymoquinone has been prepared directly from thymol by sulfonating and oxidizing the sulfonation mixture with manganese dioxide [1] or potassium dichromate; [2] the same process has been successfully applied to carvacrol.[3] The oxidation of salts of aminothymol with dichromate,[4] ferric chloride,[5] or nascent bromine [6] also leads to satisfactory yields of thymoquinone. The above procedure is based on the observation [7] that the diazonium salt obtained from aminothymol is almost quantitatively con-

verted into thymoquinone on warming in presence of excess of nitrous acid.

[1] Ann. **101**, 120 (1857).
[2] Pharm. Rev. **26**, 329 (1909) (Chem. Zentr. **1910**, I, 24).
[3] J. prakt. Chem. (2) **15**, 410 (1877); Bull. soc. chim. (3) **7**, 34 (1892).
[4] Ber. **18**, 3194 (1885).
[5] Ber. **10**, 297 (1877); Ann. **279**, 371 (1894).
[6] J. prakt. Chem. (2) **23**, 172 (1881).
[7] Ann. **279**, 371 (1894); Pharm. Rev. **26**, 364 (1909) (Chem. Zentr. **1910**, I, 24).

# XXVIII

## TRIMETHYLGALLIC ACID




Submitted by F. MAUTHNER.
Checked by H. T. CLARKE.

### 1. Procedure

To a cold solution of 80 g. (2 moles) of sodium hydroxide in 500 cc. of water in a 1-l. flask is added 50 g. (0.266 mole) of gallic acid. The flask is immediately tightly stoppered (Note 1), and the mixture shaken occasionally until all the acid has dissolved; 89 g. (67 cc.) of methyl sulfate (0.71 mole) is then added (Note 2) and the flask is shaken for twenty minutes, being cooled by means of cold water in order that the temperature does not rise above 30–35°. Occasionally the stopper is raised to release any pressure. A second portion of 89 g. of methyl sulfate is then added and shaking continued for ten minutes longer. During this second addition the temperature may rise to 40–45°.

The flask is then fitted with a reflux condenser and the contents boiled for two hours. In order to saponify the small amount of ester which is produced, a solution of 20 g. of sodium hydroxide in 30 cc. of water is then added and boiling continued

for two additional hours. The reaction mixture is then cooled and acidified with dilute hydrochloric acid; the precipitated trimethylgallic acid is filtered with suction and washed well with cold water. The product, which melts at 157–160°, is sufficiently pure for many purposes. It weighs 50–52 g. (89–92 per cent of the theoretical amount). It may be purified by recrystallization from 2 l. of boiling water with the use of decolorizing carbon, the filtration being carried out in a steam-jacketed funnel. In this way 41–43 g. (Note 3) of colorless needles melting at 167° is obtained.

## 2. Notes

1. The alkaline solution immediately darkens somewhat, owing to the presence of dissolved air; further oxidation must be limited by preventing access of air to the mixture. This is particularly necessary during the early stages; with increasing methylation the tendency to absorb oxygen falls off rapidly.

Access of air may be prevented in an apparatus that permits of mechanical stirring. For this purpose a three-necked flask is provided with a mechanical stirrer, separatory funnel and Bunsen valve. The valve is made by cutting a vertical slit in a piece of rubber tubing, closed at one end by a solid glass plug or pinchcock and attached at the other end to a piece of glass tubing contained in a stopper. Such a valve acts in one direction, permitting release of gas pressure.

2. The toxic nature of methyl sulfate vapor must always be borne in mind.

3. A further quantity can be recovered by concentrating the mother liquor. The residue of decolorizing carbon is also likely to contain an appreciable proportion of trimethylgallic acid, which can be extracted by boiling it with the mother liquor.

## 3. Other Methods of Preparation

Trimethylgallic acid is most conveniently prepared by methylating gallic acid with methyl sulfate.[1] It has also been obtained

by methylating methyl gallate and saponifying the product,[2] and by the oxidation of various natural products.[3] It has been found in nature.[4]

[1] Ann. **340**, 219 (1905); J. Chem. Soc. 89, 1655 (1906); **111**, 7 (1917); Ber. **45**, 2718 (1912); J. Am. Chem. Soc. **36**, 517 (1914).

[2] Ber. **21**, 2022 (1888).

[3] Ber. **34**, 3009 (1901); **41**, 1771 (1908).

[4] J. Chem. Soc. **95**, 253 (1909).

XXIX

# TRIMYRISTIN

Ether Extraction of Nutmegs →

$$CH_2(OCOC_{13}H_{27})CH(OCOC_{13}H_{27})CH_2(OCOC_{13}H_{27})$$

Submitted by G. D. BEAL.
Checked by H. T. CLARKE and E. R. TAYLOR.

## 1. Procedure

IN the container *A* (Fig. 5)* is placed 1500 g. of crushed nutmegs (Note 1) moistened with ether (Note 2). *A* is a 3-l. inverted aspirator bottle connected by a 3-mm. glass tube to the efficient condenser *C*, and by 3-mm. tubing, one end of which is provided with a cotton filter, to the 2-l. round-bottom flask *B*. Flask *B* is connected by 3-mm. tubing of 75 cm. length to *C*. In *B* are placed 500 cc. of ether and a few chips of clay plate to prevent superheating. *B* is then heated on a steam cone so that the ether boils rapidly enough to reach the condenser *C* and to flow back through *A*.

The extraction with ether is continued until the ether leaving the insoluble solid is entirely colorless. This requires twenty-four to seventy-two hours, according to the state of subdivision of the nutmegs and the rate at which the ether is passed through. The ethereal solution is then freed of a small quantity of entrained insoluble matter by filtering through a folded paper. This filtration may advantageously be completed in the type of extractor described in Org. Syn. **2**, 49. The clear solution is now entirely freed from ether by distillation on the water bath. The residue weighs 640–690 g. On cooling it sets to a mass of crystals of trimyristin which is filtered with

* This modified Soxhlet extractor was devised by D. F. McFarland.

suction (Note 3) and washed with 225 cc. of cold 95 per cent ethyl alcohol in small portions. The product is now recrystallized from 3.5 l. of 95 per cent ethyl alcohol; it is stirred mechanically during cooling since the trimyristin tends to separate as an oil at the outset (Note 4). The crystallized trimyristin is then filtered off by suction and washed with 350–400 cc. of 95 per cent alcohol in small portions. The crystals, which are colorless and practically odorless, melt at 54–55°. The yield is 330–364 g.

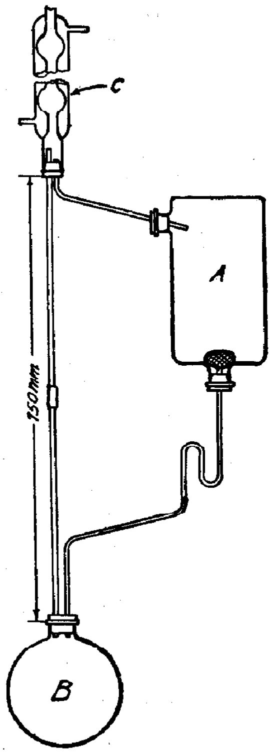



Fig. 5.

## 2. Notes

1. If the nutmegs be crushed to No. 40 powder, as recommended by the authors, the extraction is complete in twenty-four to forty-eight hours; in checking it was found more convenient merely to pass the nutmegs through a food chopper (whereby they were broken up into pieces the largest of which were 3–4 mm. across), when the extraction required sixty-six to seventy-two hours for completion.

If nutmeg butter, a commercial fat obtained by the hot pressing of ground nutmegs, is available, the above extraction may be omitted. The only operation necessary is a double crystallization of the crude material from boiling 95 per cent alcohol. Since nutmeg butter is frequently adulterated with foreign fats, the purity of the product should be checked by the saponification number (232 for pure trimyristin).

2. The nutmeg must first be moistened with ether, otherwise the extraction takes much longer. The author has found this apparatus to be generally satisfactory for the extraction of vegetable drugs with volatile solvents.

3. The filtrate from the crude trimyristin contains the odorous oils of the nutmeg. A further quantity of trimyristin may be obtained from it by distilling with steam and recrystallizing the non-volatile residue twice from alcohol; but the amount is not commensurate with the trouble, and this operation is not advised unless the residues from at least 5000 g. of nutmegs are on hand.

4. The alcohol may be distilled from the mother liquor of the recrystallization. The residue from this distillation may be added to the mother liquor of the first crystallization, which is then concentrated to the crystallization point. The crop of crystals thus obtained will usually require double recrystallization. Alcohol recovered from the first mother liquor will contain too much volatile oil of nutmeg to be used for other purposes.

## 3. Other Methods of Preparation

The only convenient source of trimyristin is nutmegs, and ether is the most suitable solvent for its extraction.[1] It has also been prepared from glycerol and myristic acid.[2]

[1] Ann. **37**, 152 (1841); **202**, 172 (1880); J. Chem. Soc. **93**, 1653 (1908). *Cf.* Ber. **12**, 1668 (1879).

[2] Rec. trav. chim. **18**, 197 (1899).

# ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parenthesis following the name of a compound refer to the volume and page of Organic Syntheses.)

**Allyl alcohol** (1, 15).—When the crude allyl alcohol is distilled from a steam bath under reduced pressure, the distillate is considerably richer in allyl alcohol (sometimes up to 90 per cent) than according to the original directions. The strength can be readily determined by measuring the specific gravity and comparing with the following figures:

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Per cent allyl alcohol.. | 65 | 70 | 75 | 80 | 85 | 90 | 95 | 100 |
| Density at 20°........ | .920 | .911 | .902 | .893 | .884 | .875 | .865 | .854 |

The best results are obtained when working at a pressure of 200-300 mm. Some boiling points of the watery alcohol are: 60°/200 mm., 70°/300 mm. and 78°/500 mm.

**Benzoin** (1, 33).—The reaction sometimes takes place with considerable violence and material may be lost through the condenser. Accordingly a somewhat larger flask is generally desirable or the upper end of the reflux condenser is provided with a wide tube leading to an empty flask. (Private communication by several.)

**p-Bromophenol** (1, 39).—Line 12 on page 42 should read: " Holleman and Rinkes [7] have recently studied the bromination, etc."

**9, 10-Dibromoanthracene** (3, 41).—When recrystallized from xylene, samples have been obtained that melt as high as 226° (uncorr.). E. de Barry Barnett (private communication).

**Furfural** (1, 49).—The low yield of furfural from straw and other materials makes it desirable to extract the aqueous furfural distillate after acid hydrolysis by a solvent heavier than

water, such as chloroform. This is done by adding a funnel to the end of the condenser so that the distillate passes directly into a layer of chloroform contained in a receiver. Distillation is continued until the chloroform layer does not increase. The furfural is obtained by distillation of the chloroform layer, and practically all of the chloroform is recovered. From the laboratory of H. I. Waterman (private communication).

**Methylene iodide** (1, 57).—The methylene iodide obtained after vacuum distillation melts at 6°.

**p-Nitrobenzoyl chloride** (3, 75).—*p*-Nitrobenzoic acid is heated under reflux with an excess of thionyl chloride. After the excess thionyl chloride has been distilled at atmospheric pressure, the *p*-nitrobenzoyl chloride is distilled under reduced pressure. Excellent results are reported by Joseph Kenyon (private communication).

# LATER REFERENCES TO PREPARATIONS IN PRECEDING VOLUMES

(The following references are to methods of preparative value that have been described up to 1926. The numbers in parenthesis following the name of a compound refer to the volume and page of *Organic Syntheses*.)

**Acetal** (3, 1):

(*a*) By passing acetylene into alcohol containing sulfuric acid and mercuric sulfate. REICHERT, BAILEY and NIEUWLAND, J. Am. Chem. Soc. **45**, 1552 (1923).

(*b*) A general method for preparing acetals by treating aldehydes or ketones with the appropriate tetra-alkyl silicate, using dry hydrogen chloride as the catalyst. HELFERICH and HAUSEN, Ber. **57**, 795 (1924).

**Allyl alcohol** (1, 15):

From oxalic acid and glycerol. COFFEY and WARD, J. Chem. Soc. **119**, 1301 (1921).

**Benzalacetone** (3, 17):

By a modified Claisen condensation. LEWINSOHN, Perfumery Essent. Oil Record **15**, 118 (1924) (C. A. **1924**, 2222).

**Benzalacetophenone** (2, 1):

From benzaldehyde, acetophenone, and hydrogen chloride in glacial acetic acid. STRAUS and GRINDEL, Ann. **439**, 276 (1924).

**Benzoic anhydride** (3, 21):

From benzoic acid and acetic anhydride. AUTENRIETH and THOMAE, Ber. **57**, 431 (1924).

**Cyclohexene** (5, 33):

From cyclohexanol and a small amount of sulfuric acid. SENDERENS, Compt. rend. **177**, 1183 (1923).

**Cyclohexene oxide** (5, 35):

From chlorocyclohexanol and alkalies. GODCHOT and BEDOS, Bull. soc. chim. (4), **37**, 1454 (1925).

**Diacetone alcohol** (1, 45):

(*a*) From acetone and sodium hydroxide. LOCQUIN, Ann. chim. (9), **19**, 32 (1923).

(*b*) From acetone and lime. EDMONDS, U. S. pat. 1,550,792 (1925) (C. A. **1926**, 51).

**Ethyl cyanoacetate** (3, 53):

From ethyl chloroacetate and sodium cyanide, and by esterifying cyanoacetic acid. STEPHENS, J. Soc. Chem. Ind. **43**, 313T, 327T (1924).

**Ethyl oxalate** (2, 22, and 5, 59):

By passing vapors of ethyl alcohol through oxalic acid. DUTT, J. Chem. Soc. **123**, 2714 (1923).

**Furfural** (1, 49):

(*a*) From cellulose. RICARD, U. S. pat. 1,322,054 (1919) (C. A. **1920**, 284); Can. pat. 220,474 (1922) (C. A. **1922**, 2868). CLAASEN, Ger. pat. 376, 418 (1923) (Chem. Zentr. **1923**, II, 540).

(*b*) From rice. SCURTI and ZAY, J. Soc. Chem. Ind. **39**, 441A (1920).

(c) From corncobs. LA FORGE, J. Ind. Eng. Chem. **13**, 1024 (1921); **15**, 499 (1923). LA FORGE and MAINS, Ind. Eng. Chem. **15**, 1057 (1923); **16**, 356 (1924).

(*d*) From acetylene, water and iron. STEUER and GROB, U. S. pat. 1,421,743 (1922) (C. A. **1922**, 3093).

(*e*) From xylan. HEUSER and SCHERER, Brennstoff-Chemie, 4, 97 (1923) (Chem. Zentr. **1923**, I, 1489).

(*f*) From pentosan in wood. GIERISCH, Cellulosechemie, **6**, 61 (1925) (Chem. Zentr. **1925**, II, 1822).

(*g*) Reviews of preparation and properties. MONROE, J. Ind. Eng. Chem. **13**, 133 (1921); MINER, TRICKEY and BROWNLEE, Chem. Met. Eng. **27**, 299, 362 (1922); ZEPF, Die Metallbörse **13**, 1227 (1923) (Chem. Zentr. **1923**, II, 945); VAN OS, Chem.

Weekblad, **22**, 18 (1925) (Chem. Zentr. **1925**, I, 1076); "Furfural and its Derivatives," Miner Laboratories, Chicago, Ill., Bull. 2, Sept., 1925.

**Mesityl oxide** (1, 53):

(*a*) From diacetone alcohol and hydrochloric acid. HOFFMAN, U. S. pat. 1,474,035 (1923) (C. A. **1924**, 401).

(*b*) From diacetone alcohol and oxalic acid. LOCQUIN, Ann. chim. (9) **19**, 32 (1923).

**Methylamine** (3, 67):

(*a*) From acetamide and bleaching powder. BADER and NIGHTINGALE, U. S. pat. 1,489,380 (C. A. **1924**, 1836).

(*b*) Purified through its benzal derivative. SOMMELET, Compt. rend. **178**, 217 (1924). (This method has been checked and found satisfactory by one of the editors.)

**Methylene iodide** (1, 57):

From methylene chloride and potassium iodide. PERKIN and SCARBOROUGH, J. Chem. Soc. **119**, 1400 (1921).

**Nicotinic acid** (4, 49):

Essentially the method given in Organic Syntheses. MCELVAIN and ADAMS, J. Am. Chem. Soc. **45**, 2738 (1923).

**p-Nitrobenzoic acid** (2, 53):

(*a*) By electrolytic oxidation of *p*-nitrotoluene. DUNBROOK and LOWY, Trans. Am. Electrochem. Soc. **45** (pre-print) (1924) (C. A. **1924**, 1088).

(*b*) From oxidation of *p*-nitrotoluene by nitric acid. LLOYD and GERSHON, U. S. pat. 1,458,715 (C. A. **1923**, 2587).

**n-Propylbenzene** (4, 59):

From benzylmagnesium chloride and ethyl *p*-toluenesulfonate. GILMAN and BEABER, J. Am. Chem. Soc. **47**, 518 (1925).

**o-Tolunitrile and p-Tolunitrile** (4, 69):

Essentially the method given in Organic Syntheses. CLARKE and READ, J. Am. Chem. Soc. **46**, 1001 (1924).

**Trimethylamine** (1, 75):

From ammonia, formaldehyde and formic acid. SOMMELET and FERRAND, Bull. soc. chim. (4) **35**, 446 (1924). (This method has been checked by one of the editors and is highly recommended.)

**Trimethylene bromide** (1, 8):

From trimethylene glycol and hydrogen bromide. KAMM and NEWCOMB, J. Am. Chem. Soc. **43**, 2228 (1922).

**Trimethylamine hydrochloride** (1, 79):

(*a*) From ammonium chloride and methyl alcohol. TURNER and HOWALD, J. Am. Chem. Soc. **42**, 2663 (1920).

(*b*) From ammonia and methyl alcohol with a catalyst. BROWN and REID, J. Phys. Chem. **28**, 1067 (1921).

**Triphenylmethane** (4, 81):

Essentially the method given in Organic Syntheses. NORRIS and YOUNG, J. Am. Chem. Soc. **46**, 2580 (1924).

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# SUBJECT INDEX

(This index comprises material from all volumes of this series.)

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# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS



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VOL. VII


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# PREFACE TO VOLUME VII

THE general plan of this series as set forth in the preceding volumes has been followed in the present volume. It is a great pleasure to acknowledge the help of former and new contributors both in this and other countries. In this volume twenty-six of the thirty preparations have been submitted by twenty-four contributors, four of whom are of foreign countries.

Of the special features included in previous volumes, all have been retained except the collection of later references to preparations in preceding volumes. This will appear again in Volume VIII. A few corrections to some of the earlier preparations are included in the Appendix. The editors acknowledge their appreciation of the help given by those submitting the corrections, and invite any comments on the preparations in any of the volumes.

In the present volume, seventeen of the preparations use as starting materials substances for which directions appear in this or earlier volumes. By the use of these preparations it is possible to arrange interesting series of preparations each of which starts from the product of the preceding one.

In addition to all other thanks which are due, the editor-in-chief of this volume wishes to thank his colleague, Louis Ehrenfeld, for his invaluable assistance especially in checking all computations.

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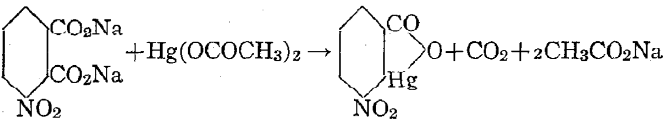
## ANHYDRO-2-HYDROXYMERCURI-3-NITROBENZOIC ACID



Submitted by FRANK C. WHITMORE, P. J. CULHANE and H. T. NEHER
Checked by HENRY GILMAN and C. C. VERNON.

### 1. Procedure

A SOLUTION of 80 g. (2 moles) of sodium hydroxide in 800 cc. of water is prepared in a 2-l. beaker. To the warm solution is added 211 g. (1 mole) of 3-nitrophthalic acid (p. 70) (Note 1). A small amount of insoluble material is removed by filtration through a large preheated Büchner funnel (Note 2). A solution of 350 g. (1.1 moles) of mercuric acetate (Note 3) in a mixture of 50 cc. of glacial acetic acid and 700 cc. of water is prepared by heating and filtering while hot (Note 4). The two hot solutions are poured into a 3-l. long-necked flask and mixed by shaking. No precipitate should separate (Note 5). The flask is clamped in a large oil bath (Note 6) with the level of the oil almost to the neck of the flask. It is fitted with a reflux condenser provided with a tube leading to a large beaker placed on the desk (Note 7). The temperature of the oil bath is raised to 170° over a period of about one hour. If any considerable amount of material

is driven through the condenser, it is poured back through the top of the condenser as soon as the reaction slackens. The heating at 165–175° is continued for about seventy hours. After about sixty hours the end of the tube leading from the top of the condenser is introduced below the surface of about 1 cc. of mercury in a small test tube. The evolution of carbon dioxide can be followed by observing the bubbles which pass through the mercury. When not more than one or two bubbles escape per minute, the heating is discontinued (Note 8).

The product is allowed to settle and the hot supernatant liquid is poured through a preheated suction filter. The filtrate deposits less than 10 g. of crude product on cooling. The product in the flask is shaken with several 100-cc. portions of water, and all the fine material is transferred to the filter. Some lumpy material is usually left in the flask. This is transferred to a large mortar and ground to a paste with a little water and then transferred to the filter. After sucking as dry as possible, the suction is shut off, and 100 cc. of alcohol is poured over the material on the filter. After standing a few minutes, suction is again applied. The product is then dried to constant weight (Note 9). The yield of anhydro-2-hydroxymercuri-3-nitrobenzoic acid is 300–330 g. (82–90 per cent of the theoretical amount based on the 3-nitrophthalic acid used). It is a cream-colored powder which dissolves in an excess of dilute sodium hydroxide, leaving only a slight turbidity (Notes 10 and 11).

## 2. Notes

1. 3-Nitrophthalic acid melting above 200° (sealed tube) is pure enough for this preparation.

2. Although the insoluble material is very small in amount, filtration without suction is too slow.

3. Commercial mercuric acetate, about 90 per cent pure, was used. The equivalent amounts of mercuric oxide and acetic acid may be used if the acetate is not available.

4. A small amount of mercurous compounds is removed by the filtration.

5. If more concentrated solutions are used, the mercuric salt precipitates and the reaction runs less smoothly.

6. A large galvanized pail containing extra heavy lubricating oil was used. This oil does not fume even after heating for long periods.

7. This beaker serves to catch any material which is carried over during a slightly violent reaction which sometimes takes place at the beginning.

8. If a more accurate indication of the end of the reaction is desired, a tube of mercury may be inverted in a small beaker of mercury and any gas evolved during the later stages of the reaction may be collected over the mercury.

9. The wet material may be used without drying for the preparation of 2-bromo-3-nitrobenzoic acid (p. 12).

10. To dissolve the mercury compound it should be dusted into boiling sodium hydroxide solution.

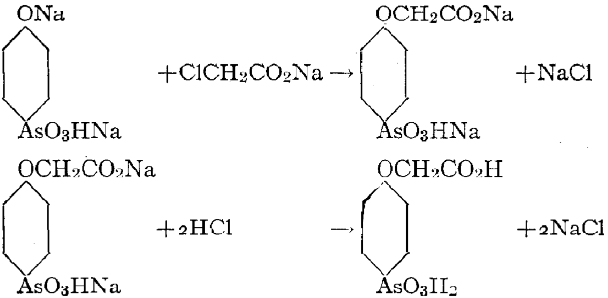
11. By a similar procedure phthalic anhydride may be converted into anhydro-o-hydroxymercuribenzoic acid. Thus, 300 g. (2 moles) of phthalic anhydride and 750 g. (2.2 moles) of commercial mercuric acetate (Note 3) gives 550 g. of the mercury compound (85 per cent of the theoretical amount). With phthalic anhydride the reaction is complete in six to ten hours.

### 3. Other Methods of Preparation

The preparation of anhydro-2-hydroxymercuri-3-nitrobenzoic acid does not appear in the literature.

## II

## *p*-ARSONOPHENOXYACETIC ACID




Submitted by C. S. PALMER and E. B. KESTER.
Checked by J. B. CONANT.

### 1. Procedure

IN a 2-l. round-bottom flask is placed 218 g. (1 mole) of *p*-hydroxyphenylarsonic acid (Note 1) and 375 cc. of water. A solution of 180 g. (4.5 moles) (Note 2) of sodium hydroxide in 375 cc. of water is added, and the mixture shaken until a homogeneous solution is obtained. After cooling to 40–50° there is added 189 g. (2 moles) of chloroacetic acid in small portions (Note 3) with stirring, and the clear solution is refluxed for four hours. At the end of this time the mixture is cooled to 20°, filtered to remove a slight flocculent precipitate, and the *p*-arsonophenoxyacetic acid precipitated (Note 4) by the addition of 200 cc. (2.1 moles) of hydrochloric acid (sp. g. 1.19). The product is filtered on a 10-cm. Büchner funnel and washed with three successive 100-cc. portions of cold water. It is then crystallized from 2 l. of hot water (Note 5), filtered, and washed

twice with 100-cc. portions of cold water, once with 25 cc. of acetone, and once with 25 cc. of ether. After drying at 110° for one hour, there remains a pure white, anhydrous product weighing 110–120 g. (40–43 per cent of the theoretical amount) (Note 6). An arsenic analysis shows the product to be about 99 per cent pure.

## 2. Notes

1. Commercial phenolarsonic acid may be used, or 240 g. of sodium *p*-hydroxyphenylarsonate (Org. Syn. **4**, 65) and 140 g. of sodium hydroxide may be substituted for the acid and the larger amount of base.

2. The use of less than 4.5 moles of alkali lowers the yield, while an increase in the alkali concentration does not increase the yield.

3. Unless the chloroacetic acid is added cautiously, there may be a violent reaction and the yield of *p*-arsonophenoxyacetic acid is lowered.

4. The product sometimes does not precipitate readily without vigorous agitation and rubbing the inside wall of the vessel with a stirring rod.

5. It is sometimes necessary to use decolorizing carbon in order to get a white recrystallized product.

6. The odor of phenol is strong at the end of the reaction, but most of the *p*-hydroxyphenylarsonic acid which does not react with the chloroacetic acid is not hydrolyzed and can be recovered in the filtrate from the *p*-arsonophenoxyacetic acid.

## 3. Other Methods of Preparation

*p*-Arsonophenoxyacetic acid has been made by heating aqueous sodium *p*-hydroxyphenylarsonate, two moles of chloroacetic acid, and four moles of sodium hydroxide.[1]

[1] Ger. pat. 216,270; Frdl. **9**, 1047 (1908–10).

## III

## BENZANILIDE

$$C_6H_5NH_2 + C_6H_5CO_2H \rightarrow C_6H_5NHCOC_6H_5 + H_2O$$

Submitted by CARL N. WEBB.
Checked by C. S. MARVEL and P. L. SALZBERG.

### 1. Procedure

IN a 3-l. round-bottom flask are placed 750 g. (8.1 moles) of aniline (Note 1) and 1 kg. (8.2 moles) of benzoic acid. When about two-thirds of the benzoic acid is in the flask the mixture is melted to make room for the rest. The flask is placed in a large oil bath and connected to a condenser for distillation. The temperature of the oil is raised quickly to 180–190°, at which point distillation starts. The bath is held at this temperature until practically no more aniline and water distil (about two hours), and then the temperature is slowly raised to 225° and maintained at this temperature until no further distillation takes place (one to two hours). The oil bath is now removed and the contents of the flask are allowed to cool below 180° and 550 g. (5.9 moles) of aniline is added. The distillations at 190° and 225° are repeated (about six hours). The hot mixture is poured into two 20-cm. evaporating dishes (hood) and is allowed to cool. The crude product weighs 1600–2000 g., depending on the amount of aniline retained.

The purplish-gray solid is ground (Note 2) in a large mortar and is poured with vigorous stirring into a 12-l. (3-gal.) crock containing 6 l. of approximately normal hydrochloric acid (5.5 l. of water and 500 cc. of concentrated hydrochloric acid). The stirring is continued for one hour after all the benzanilide has been added, and then the solid is filtered on a 20-cm. Büchner funnel. The process of stirring with acid and filtering is repeated twice to remove the excess of aniline. The solid is stirred for two hours with 6 l. of water and is filtered. It is stirred for one

hour with 6 l. of normal sodium hydroxide solution to remove the excess of benzoic acid and is then filtered. The stirring with alkali and filtering is repeated. The solid is next stirred for two hours with 7 l. of water and is filtered, sucked dry, and air-dried over night on paper.

After drying on paper the purplish solid is dried to constant weight in three 20-cm. evaporating dishes at 90–100° (about two days) and is then repowdered. The product is light purplish-gray and weighs 1270–1325 g. (80–84 per cent of the theoretical amount). It melts at 157–160°. The product is pure enough for use in the preparation of *p*-dimethylaminobenzophenone (p. 24) and for most synthetic purposes. When 100 g. of benzanilide is dissolved in 750 cc. of hot alcohol (Note 3) and the solution is boiled with about 10 g. of decolorizing carbon (Norite), filtered, and cooled to 10° over night, 80–86 g. of an almost colorless product melting at 160–161° separates. A second crystallization from alcohol using decolorizing carbon gives a white product with approximately the same loss in the mother liquors as in the first crystallization.

## 2. Notes

1. The ordinary "pure" aniline of commerce gives as good yields and as pure a product as redistilled aniline.

2. The benzanilide must be finely ground in order that aniline and benzoic acid may be completely extracted.

3. Very little of the solid fails to go into solution. The hot solution must be filtered rapidly as the benzanilide crystallizes easily.

## 3. Other Methods of Preparation

Benzanilide has been prepared by the treatment of aniline with benzoyl chloride,[1] benzoic anhydride,[2] or benzoic acid.[3] The method described in the procedure is essentially that of Nägeli.

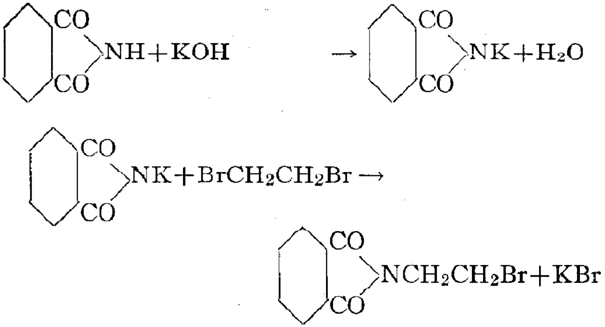
[1] Gerhardt, Ann. **60,** 311 (1846); Dehn and Ball, J. Am. Chem. Soc. **36,** 2096 (1914).

[2] Meyer and Sundmacher, Ber. **32,** 2123 (1899).

[3] Hübner, Ann. **208,** 291 (1881); Nägeli, Bull. soc. chim. [3] **11,** 892 (1894).

IV

## β-BROMOETHYLPHTHALIMIDE



Submitted by P. L. Salzberg and J. V. Supniewski.
Checked by F. C. Whitmore and H. C. Benedict, Jr.

### 1. Procedure

**A. Potassium Phthalimide.**—In a 2-l. round-bottom flask fitted with a reflux condenser are placed 80 g. (0.54 mole) of phthalimide (Note 1) and 1600 cc. of absolute alcohol. (Org. Syn. **5**, 56.) The mixture is gently boiled for about fifteen minutes or until no more of the phthalimide dissolves (Note 2). The hot solution is decanted from any solid into a specially prepared solution of 30.5 g. (0.54 mole) of potassium hydroxide (Note 3). A precipitate of potassium phthalimide separates at once. The mixture is stirred and cooled quickly to room temperature, and the precipitate is filtered with suction. To the alcoholic mother liquors a second 80-g. portion of phthalimide is added, and the entire process is repeated. The two crops of crystals are united (Note 4) and washed with 200 cc. of acetone

to remove any unchanged phthalimide. The yield of air-dried potassium phthalimide is 160–180 g. (79–89 per cent of the theoretical amount).

**B. β-Bromoethylphthalimide.**—*In a 1-l. two-necked round-bottom flask fitted with an efficient stirrer and a reflux condenser are placed 150 g. (0.8 mole) of potassium phthalimide and 450 g. (2.4 moles) of ethylene dibromide* (Note 5). The stirrer is started and the mixture is heated for about twelve hours in an oil bath maintained at 180–190°. The condenser is then set for distillation, and the excess of ethylene dibromide is distilled under reduced pressure. The recovery of the bromide amounts to 290–295 g. (Note 6).

The crude bromoethylphthalimide is extracted from the potassium bromide by refluxing with 300 cc. of alcohol (98–100 per cent) (Note 7) until the dark oil is entirely dissolved. This requires about one-half hour. The hot solution is filtered with suction, and the residue of salt is washed with a little hot alcohol. The alcohol is distilled under reduced pressure, and the dry residue is refluxed with 500 cc. of carbon disulfide for about fifteen minutes in order to separate the soluble bromoethylphthalimide from the insoluble diphthalimidoethane (Note 8). The warm solution is filtered with suction. The carbon disulfide is distilled under diminished pressure (Note 9). The bromoethylphthalimide remains as light tan crystals which melt at 78–80°. *The yield is 140–160 g. (69–79 per cent of the theoretical amount).*

The product thus obtained is pure enough for most purposes. However, a purer product may be obtained by recrystallization from dilute alcohol in the presence of decolorizing carbon. When 50 g. of crude product is dissolved in 200 cc. of 75 per cent alcohol, boiled for about ten minutes with 5 g. of decolorizing carbon (Norite), filtered, and the solution cooled to 0°, 40 g. of white product is obtained. The recrystallized product melts at 80–81°. A second recrystallization raises the melting point to 82–83°.

## 2. Notes

1. The phthalimide used was the crude product obtained as described in Org. Syn. **2**, 75.

2. The crude product always contains a small amount of material insoluble in alcohol.

3. It is convenient to prepare enough potassium hydroxide solution for the two precipitations at one time. This solution is prepared by dissolving 61 g. of potassium hydroxide in 60 cc. of water. To this solution is then added 180 cc. of absolute alcohol. One-half of the resulting solution is used for each 80-g. portion of phthalimide.

4. After the first crop has filtered, most of it should be removed and the second crop should be filtered through the same paper. The alcoholic filtrate on distillation yields about 1500 cc. of 98 per cent alcohol.

5. The ethylene dibromide which was used, boiled at 129–131°.

6. The last 15 to 20 g. of this recovered product distils very slowly.

7. The alcohol recovered from the preparation of the potassium phthalimide may be used for this extraction.

8. About 10 g. of crude diphthalimidoethane is obtained.

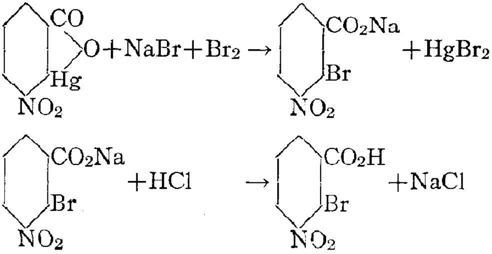
9. If the carbon disulfide is distilled at ordinary pressures, the residue melts and turns very dark. The crude yield is not lowered, but the purification is made more difficult.

## 3. Other Methods of Preparation

The method described is based on that of Gabriel.[1]

[1] Ber. **20**, 2224 (1887); **21**, 566 (1888); **22**, 1137 (1889)

# 2-BROMO-3-NITROBENZOIC ACID



Submitted by PAUL J. CULHANE.
Checked by HENRY GILMAN and C. C. VERNON.

## 1. Procedure

A SOLUTION of 50 g. (1.25 moles) of sodium hydroxide in 1.5 l. of water is prepared in a 5-l. flask, and the solution is heated to gentle boiling. To the hot solution is added, in small quantities, 330 g. (0.9 mole) of anhydro-2-hydroxymercuri-3-nitrobenzoic acid (p. 1) (Note 1). The mixture is stirred after the addition of each portion of about 50 g. until the material has gone into solution except for a small residue. The flask is then fitted with a stirrer and addition tube (Note 2) and with a connection to a reflux condenser. The material is heated to boiling and stirred vigorously. There is slowly added with continuous stirring 85 cc. (0.95 mole) (Note 3) of concentrated hydrochloric acid (sp. g. 1.19). Heating is discontinued at this point, and 30 cc. (0.5 mole) of glacial acetic acid (sp. g. 1.05) (Note 3) is added slowly. A curdy precipitate forms.

A solution of bromine is prepared by dissolving 103 g.

(1 mole) of sodium bromide and 160 g. (55 cc., 1 mole) of dry bromine in 150 cc. of water (Note 4). The mixture is stirred, and the bromine solution is added as rapidly as possible through the shaft of the stirrer. The precipitate dissolves. The solution is heated to boiling for five minutes after the last of the bromine has been added. The solution is then made slightly alkaline by the addition of 20 g. (0.5 mole) of solid sodium hydroxide and filtered through a fluted filter. The filtrate is then made acid to Congo Red, using about 150 cc. of concentrated hydrochloric acid. The precipitated 2-bromo-3-nitrobenzoic acid is filtered with suction and sucked as dry as possible. It is then crystallized from 1 l. of hot 30 per cent alcohol. The yield of product melting at 185–187° is 130–150 g. (53–61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used). About 25 g. of material melting at about 175° can be recovered from the mother liquor.

## 2. Notes

1. The reaction product from the mercuration of 3-nitrophthalic acid (1 mole) is used. The mercury compound can be used without drying if desired. If this is done, solution takes place much more readily.

2. A rapid distribution of the added material is necessary to prevent a local excess of the reagent added. This is very important when hydrochloric acid is added, as this tends to decompose the mercury compound. A convenient arrangement consists of a 3-way tube of about 15-mm. bore. The stirrer operates through the center tube. The other arms are used for the condenser and for the addition of material. A three-necked flask provided with a long-stemmed separatory funnel reaching below the stirrer may be used.

3. The addition of one mole of hydrochloric acid allows the formation of one mole of sodium chloride, which is of advantage in the subsequent addition of halogen, owing to the formation of a sodium salt of the chloromercuric acid, this being more soluble and hence more reactive than the anhydro compound. Acetic

acid is used for the final acidification because it does not decompose the mercury compound. The replacement by bromine takes place best in a slightly acid medium.

4. The mercury can be replaced by iodine in a similar manner. An iodine solution is made by dissolving 166 g. (1 mole) of potassium iodide and 255 g. (1 mole) of iodine in 250 cc. of water. This is used instead of the bromine solution. The mixture is filtered from the mercuric iodide and the filtrate acidified with 200 cc. of concentrated hydrochloric acid. The precipitate is filtered and then stirred with a solution of 10 g. of potassium iodide in 250 cc. of water to remove mercuric iodide. The mixture is filtered with suction and the precipitate crystallized from 1 liter of 50 per cent alcohol. The yield is 180 g. of 2-iodo-3-nitrobenzoic acid melting at 204–205.5° (61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used).

### 3. Other Methods of Preparation

2-Bromo-3-nitrobenzoic acid has been prepared by the nitration of 2-bromobenzoic acid, the 2,3 acid being separated from the 2,5 acid, which is the principal product of the nitration, by fractional crystallization of the potassium salts from water.[1]

2-Iodo-3-nitrobenzoic acid has been prepared by the diazotization of 3-nitro-anthranilic acid.[2]

[1] Holleman and de Bruyn, Rec. trav. chim. **20**, 211 (1901).

[2] James, Kenner and Stubbings, J. Chem. Soc. **117**, 776 (1920).

## CHLOROACETAMIDE

$$ClCH_2CO_2C_2H_5 + NH_3 \rightarrow ClCH_2CONH_2 + C_2H_5OH$$

Submitted by W. A. Jacobs and M. Heidelberger.
Checked by C. S. Marvel and D. D. Coffman.

### 1. Procedure

In a 2-l. round-bottom flask fitted with a mechanical stirrer and surrounded by an ice-salt bath is placed 215 g. (1.75 moles) of ethyl chloroacetate (Note 1). Vigorous stirring is started and to the cold ester (Note 2) 200 cc. of chilled aqueous ammonia (sp. g. 0.9) is added. The solution is stirred in the cold for about fifteen minutes; then another 200-cc. portion of aqueous ammonia is added, and the stirring continued for about fifteen minutes. The mixture is then allowed to stand for thirty minutes, filtered with suction, and washed with two 25-cc. portions of cold water to remove ammonium chloride. The yield of air-dried material melting at 118–119° (Note 3) is 128–138 g. (78–84 per cent of the theoretical amount).

This product contains traces of ammonium chloride which may be removed by crystallization from water. When 100 g. of crude product is recrystallized from 400 cc. of water, about 80 g. of product is obtained. The recrystallized product melts at 119–120°.

1. The ethyl chloroacetate used may be a commercial grade which boils at 141–146°. The ethyl chloroacetate and the chloroacetamide have the usual irritating effect of chloroacetyl compounds.

2. The temperature is best maintained at 0–5°. At higher temperatures there is more replacement of the chlorine and the yields are considerably lower.

3. Traces of moisture lower the melting point considerably.

### 3. Other Methods of Preparation

Chloroacetamide has been prepared from chloroacetyl chloride and dry ammonia gas,[1] and by the treatment of ethyl chloroacetate[2] or methyl chloroacetate[3] with cold aqueous ammonia solutions. The directions given above were developed from the methods of Scholl[2] and Tröger and Hille.[2]

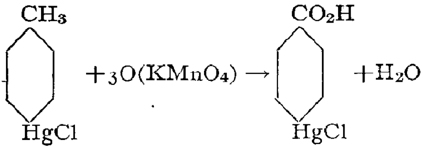
[1] Willm, Ann. **102**, 110 (1857).

[2] Willm, Ann. **102**, 110 (1857); Menschutkin and Jermoljew, Z. Chem. **1871**, 5; Bauer, Ann. **229**, 165 (1885); Scholl, Ber. **29**, 2417 (1896); Tröger and Hille, J. prakt. Chem. (2) **71**, 204, (1905).

[3] Henry, Rec. trav. chim. **24**, 165 (footnote 3) (1905).

VII

## p-CHLOROMERCURIBENZOIC ACID




Submitted by FRANK C. WHITMORE and GLADYS E. WOODWARD.
Checked by HENRY GILMAN and J. D. ROBINSON.

### 1. Procedure

FIVE hundred grams (1.6 moles) of crude *p*-tolylmercuric chloride (Org. Syn. **3**, 99) and 720 g. (4.5 moles) of potassium permanganate are added to a solution of 1200 g. (30 moles) of sodium hydroxide in 18 l. of water contained in a large enamelled pail (or similar vessel) placed on a 15-cm. (6-in.) Fletcher burner and provided with a mechanical stirrer. The mixture is stirred and heated as near boiling as possible for fifteen minutes. The highest temperature conveniently obtainable is 95°. The tolylmercuric chloride dissolves (Note 1), forming the sodium salt of *p*-hydroxymercuribenzoic acid. The solution is cooled somewhat and alcohol is added to react with the excess of potassium permanganate (250 cc. is generally required to completely decolorize the solution). The manganese dioxide thus precipitated is removed by filtering with suction (Note 2). The filtrate should be clear and colorless. (If it is green, not enough alcohol has been added.) After the filtrate has become thoroughly cool, (Note 3), it is acidified with hydrochloric acid, about 1700 cc. of technical concentrated acid being necessary. The precipitated *p*-chloromercuribenzoic acid is difficult to filter because of its

flocculent character. It is best to allow it to stand at least over night and then filter by suction after siphoning most of the clear supernatant liquid. The acid retains much water and should be dried at 110° (Note 4). The yield is 350–420 g. (61–74 per cent of the theoretical amount). The crude acid may be purified by reprecipitation with hydrochloric acid from a solution in sodium hydroxide. The crude acid is sufficiently pure for the preparation of *p*-iodobenzoic acid (p. 58). It can be used for this purpose without drying.

## 2. Notes

1. The chief impurity in the tolylmercuric chloride is mercurous chloride, which is converted to the oxide and remains in the manganese dioxide precipitate.

2. In filtering the manganese dioxide from the strongly alkaline solution, it is best to support the filter paper by means of a cloth which is cut to fit the funnel and placed under the filter paper.

3. It is necessary that the filtrate be cooled at least to 20° before acidifying to avoid the splitting of the C-Hg linkage.

4. The caked acid loses water very slowly, even at 110°. Since the chief use of the acid is in preparing the *p*-halogen compounds, it need not be dried, but can be mixed with water while still wet.

## 3. Other Methods of Preparation

*p*-Chloromercuribenzoic acid has been prepared by the present process [1] and by heating the corresponding boric acid,[2] $(HO)_2BC_6H_4CO_2H$, with mercuric chloride.

[1] Whitmore and Woodward, J. Am. Chem. Soc. **48**, 534 (1926).

[2] Michaelis, Ann. **315**, 35 (1901).

# $\alpha$-CYANO-$\beta$-PHENYLACRYLIC ACID

$$ClCH_2CO_2Na + NaCN \rightarrow NCCH_2CO_2Na + NaCl$$

$$NCCH_2CO_2Na + C_6H_5CHO \rightarrow C_6H_5CH{=}C(CN)CO_2Na + H_2O$$

$$C_6H_5CH{=}C(CN)CO_2Na + HCl \rightarrow C_6H_5CH{=}C(CN)CO_2H + NaCl$$

Submitted by ARTHUR LAPWORTH and WILSON BAKER.
Checked by J. B. CONANT and W. C. BOYD.

## 1. Procedure

**A. Preparation of Sodium Cyanoacetate Solution.**—In a 3-l. round-bottom flask is placed 250 g. (2.65 moles) of monochloroacetic acid. To this are added 100 cc. of water and 375 g. (1.3 moles) of crystalline sodium carbonate (decahydrate), (Note 1), the mixture being gently warmed. The neutralization is completed by adding sodium carbonate solution with litmus paper as an indicator. The flask is transferred to the hood, and a solution of 130 g. (2.65 moles) of sodium cyanide in 250 cc. of warm water is added in two approximately equal portions, waiting after the first addition until no further evolution of heat occurs, or the mixture ceases to boil. The cooled solution is neutralized with hydrochloric acid, using methyl orange as an outside indicator. The solution is then diluted with water to 1000 cc. and filtered; it should be of a light straw color. It can be kept for long periods of time in a stoppered bottle, although the color deepens somewhat.

**B. Condensation with Benzaldehyde.**—To 400 cc. (1.06 moles) of the sodium cyanoacetate solution is added a solution of 5 g. (0.13 mole) of sodium hydroxide in 400 cc. of water. The resulting alkaline solution is warmed to 40° and treated with 100 g. (0.94 mole) of benzaldehyde which has been shaken with sodium carbonate solution and distilled under reduced pressure. The benzaldehyde dissolves after vigorous shaking for a few minutes. After standing one hour, during which time some of the sodium cyanophenylacrylate crystallizes, the mixture is acidified with concentrated hydrochloric acid until acid to litmus and 40 cc. additional concentrated acid added, and the whole is shaken vigorously. After another hour, the crystalline cyanophenylacrylic acid is filtered on a Büchner funnel, washed thoroughly with cold water, and dried in a steam oven. It is then shaken with 100 cc. of benzene, filtered on a Büchner funnel, and further washed with 50 cc. of benzene and dried. The yield of product melting at 178–179° is 105–115 g. (65–70 per cent of the theoretical amount). This product may have a slight pinkish color, which can be removed by recrystallization from 740 cc. of alcohol or 10 l. of hot water. The recovery is about 57 per cent for alcohol and 92 per cent for water (Note 2). The melting point remains unchanged.

## 2. Notes

1. In place of the crystallized sodium carbonate, the equivalent amount of dehydrated material (138 g.) and water (240 cc.) may be used.

2. Owing to hydrolysis in alkaline or neutral solutions, it is very difficult to free the acid from a slight odor of benzaldehyde if it is recrystallized from water, but a final washing with benzene removes this odor.

## 3. Other Methods of Preparation

α-Cyanophenylacrylic acid has been prepared by the hydrolysis of the corresponding ester obtained by the condensation of benzaldehyde with cyanoacetic ester in the presence of sodium

alcoholate or acetic anhydride.[1] The direct condensation of benzaldehyde and cyanoacetic acid or its sodium salt takes place when the substances are heated[2] for some time at 180°. The most convenient method for the preparation of the acid (as the sodium or potassium salt) is by the action of benzaldehyde on an alkaline aqueous solution of sodium or potassium cyanoacetate prepared by the interaction of salts of bromoacetic[3] or chloroacetic acids[4] with potassium or sodium cyanide in aqueous solution.

[1] Carrick, J. prakt. Chem. (2) **45**, 501 (1892).
[2] Fiquet, Ann. chim. (6) **29**, 442 (1893); Bull. soc. chim. (3) **7**, 11 (1892).
[3] Clarke and Francis, Ber. **44**, 273 (1911).
[4] Lapworth and McRae, J. Chem. Soc. **121**, 1699 (1922).

## p-DIMETHYLAMINOBENZOPHENONE

$$C_6H_5CONHC_6H_5 + C_6H_5N(CH_3)_2 + POCl_3 \rightarrow$$
$$p\text{-}(CH_3)_2NC_6H_4C(NC_6H_5)C_6H_5$$
$$p\text{-}(CH_3)_2NC_6H_4C(NC_6H_5)C_6H_5 + H_2O + HCl \rightarrow$$
$$p\text{-}(CH_3)_2NC_6H_4COC_6H_5 + C_6H_5NH_2 \cdot HCl$$

Submitted by CHARLES D. HURD and CARL N. WEBB.
Checked by C. S. MARVEL and P. L. SALZBERG.

### 1. Procedure

FIVE hundred grams (2.5 moles) of dry, powdered benzanilide (p. 6), 1025 g. (8.4 moles) of technical dimethylaniline, and 525 g. (3.4 moles) of phosphorus oxychloride are mixed (Note 1) in a 3-l. round-bottom Pyrex flask (Note 2). The flask is fitted with a two-holed cork stopper which carries a reflux condenser and a thermometer. The top of the condenser is provided with a calcium chloride tube; the bulb of the thermometer reaches beneath the surface of the liquid

The flask is warmed in a water bath until the appearance of a sudden exothermic reaction (Note 3), at which point the flask must be cooled at once by rotating it underneath the surface of cold water. The cooling is continued until the thermometer indicates a temperature of 125° or less. The flask is then immersed in a bath of boiling water for about three hours, after which the mixture is cooled to about 50°, and poured slowly into 2.5 l. of warm (Note 4) dilute hydrochloric acid, made from 325 cc. (about 4 moles) of concentrated acid, contained in a large crock of about 15 l. (4 gal.) capacity. The mixture is left for about three hours until hydrolysis is complete (Note 5).

About 8 l. of water is added to precipitate the *p*-dimethylaminobenzophenone. The solution, milky at first, soon deposits sandy crystals of light green color, which are collected on a 20-cm. Büchner funnel. They are transferred to a beaker and washed with 1.5 l. of water, after which they are again collected on the filter, washed, pressed as dry as possible, and air dried. With no further purification the melting point is 88–90°. The yield is 350–390 g. An additional 85–100 g. of inferior product, m.p. 70–80°, is obtained by treating the combined filtrates with a solution of 250 g. (6.2 moles) of sodium hydroxide. This product, air-dried as before, is dissolved in 300–400 cc. of hot alcohol from which, by partial evaporation and cooling, more than half separates in good crystalline form, m.p. 88–90.5°. This material may be combined with the first product of similar melting point. The total yield is 410–440 g. (72–77 per cent of the theoretical amount) (Note 6).

The crude product melts fairly sharply, but it is colored light green. The color may be almost completely removed by recrystallization from hot alcohol. The best result is obtained by dissolving 100 g. of the crude product in 600 cc. of boiling alcohol, heating with 5 g. of decolorizing carbon (Norite), filtering, and cooling the solution in an ice-salt bath. The crystals are then separated from the mother liquor by centrifuging (Note 7). The yield of almost colorless crystals melting at 89.5–90.5° is 80 g.

## 2. Notes

1. This causes an elevation in temperature to about 50°.

2. Pyrex is essential to avoid breakage when the hot flask is cooled rapidly.

3. This exothermic reaction usually begins at 90–110°, and the temperature rises in a few seconds to about 180°. In smaller runs, e.g., with 100 g. of benzanilide, it is not advisable to cool the flask before the temperature has reached about 180°, as some benzanilide may remain unchanged. The flask and the attached condenser should be readily detachable from the sup-

porting ringstand so that the whole can be lifted and cooled quickly. A pail of cold water should be at hand for this purpose.

4. The temperature of the acid is 50° at the start and about 80° during the addition.

5. This should give a homogeneous solution. Should there be unused benzanilide, it will appear at this point and should be removed by filtration.

6. It is impracticable to obtain a further yield of ketone by the addition of more sodium hydroxide to the filtrate. Nor does it seem practical to recover the aniline and the excess of dimethylaniline.

7. If the crystals are separated by suction filtration, it is very hard to remove all of the mother liquor. When such crystals are air-dried, the alcohol evaporates and leaves the outer layer of material colored deep green.

## 3. Other Methods of Preparation

*p*-Dimethylaminobenzophenone is best prepared from benzanilide, dimethylaniline, and phosphorus oxychloride.[1] It has also been obtained by treatment of malachite green[2] with concentrated hydrochloric acid at 180°, and by the methylation of *p*-aminobenzophenone[3] with methyl iodide at 180°. Dimethyl sulfate[4] has also been used as a methylating agent. It is noteworthy that the ketone has not been prepared by the Friedel-Crafts method, nor by condensation methods using zinc chloride. These methods give vigorous reactions, but no ketone has been isolated from the complex mixtures which are formed.

[1] Ger. pat. 41,751; Frdl. **1**, 44 [1887]. Meisenheimer, Budkewicz and Kananow, Ann. **423**, 84 (1921).

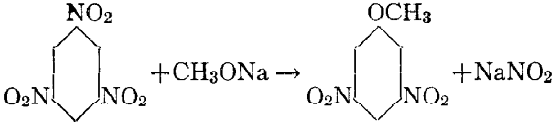
[2] Doebner, Ann. **217**, 257 (1883); Ber. **13**, 2225 (1880).

[3] Doebner, Ann. **210**, 269 (1881). Doebner and Weiss, Ber. **14**, 1837 (1881).

[4] Baeyer, Ann. **354**, 190 (1907).

# X

## 3, 5-DINITROANISOLE




Submitted by FREDERIC REVERDIN.
Checked by C. S. MARVEL and DOROTHY E. BATEMAN.

### 1. Procedure

A SOLUTION of sodium methylate is prepared by dissolving 6.3 g. (0.27 mole) of sodium in 150 cc. of absolute methyl alcohol (Note 1) in a 1-l. flask provided with a reflux condenser. To this is added a solution of 50 g. (0.23 mole) of 1,3,5-trinitrobenzene (Org. Syn. **2,** 93) in 550 cc. of absolute methyl alcohol. The mixture is boiled for about twenty minutes. The reflux condenser is then replaced by a still head and condenser, and about 300–350 cc. of alcohol is distilled. The residue in the flask is cooled to 20° and filtered. The crude product is purified by recrystallization from hot ordinary methyl alcohol. On account of the low solubility of the dinitroanisole in hot methyl alcohol, the best results are obtained by boiling the crude product with a few grams of decolorizing carbon (Norite) in about 500 cc. of methyl alcohol, filtering the hot solution through a hot funnel, cooling the solution, filtering, and using the mother liquors for another extraction. After five extractions no more of the product is dissolved. The yield of pure product melting at 105° is 29–35 g. (63–77 per cent of the theoretical amount).

## 2. Note

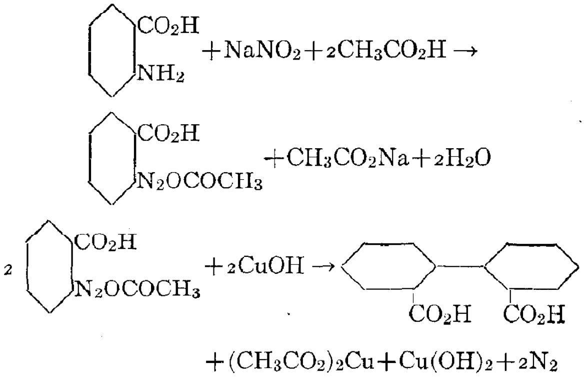
1. One liter of ordinary absolute methyl alcohol was treated with 5 g. of magnesium turnings and 0.1 g. of mercuric chloride, refluxed for ten hours, and then distilled.

## 3. Other Methods of Preparation

3,5-Dinitroanisole has been made only by this method.[1]

[1] Lobry de Bruyn, Rec. trav. chim. **9**, 208 (1890).

## DIPHENIC ACID




Submitted by E. H. HUNTRESS.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

**A. Preparation of Cuprous Hydroxide.**—Cuprous chloride is prepared from a solution of 500 g. (2 moles) of crystallized copper sulfate and 150 g. (2.55 moles) of sodium chloride in 2.5 l. of water (Org. Syn. **3**, 33) by the gradual addition of sodium sulfite (from 110 g. of sodium bisulfite). After decanting the supernatant solution, the precipitate of cuprous chloride is added to a solution of 350 cc. of 6 N sodium hydroxide in 1 l. of water contained in the 4-l. beaker in which the main synthesis is to be performed, the last portion of solid cuprous chloride being washed in with 1 l. of water. After vigorously stirring for a few minutes, the heavy precipitate of deep orange-colored cuprous hydroxide is permitted to settle and the supernatant

liquid siphoned off. The cuprous hydroxide is washed free from salt by another 2 l. of water which is not removed until the cuprous hydroxide is to be used.

**B. Diazotization of Anthranilic Acid.**—To 100 g. (0.73 mole) of anthranilic acid (m.p. 143–144°) in a 1.5-l. beaker arranged for vigorous mechanical stirring and efficient external cooling are added 300 cc. of distilled water and 133 cc. of glacial acetic acid (2.3 moles) (Note 1). A solution of 51 g. of sodium nitrite (0.74 mole) in 200 cc. of distilled water is slowly added from a separatory funnel during about forty minutes (Note 2).

**C. Synthesis of Diphenic Acid.**—When the diazonium solution is ready for use, the last wash water is siphoned from the cuprous hydroxide and the 4-l. beaker containing the latter is clamped in a 12-l. enamelled pail. The space between the beaker and the container is gradually filled with ice water as the level of the reaction mixture rises in the beaker. Provision is made for vigorous stirring of the reaction mixture, and by means of a long tube a separatory funnel is arranged to deliver the diazonium solution (Note 3) below the surface of the liquid in the beaker. Then 300 cc. of distilled water and 270 cc. (4 moles) of concentrated aqueous ammonia (sp. g. 0.90) are added (Note 4). Addition of the diazonium solution is begun at once and so regulated that all has been run in within about one hour. The thick foam is broken from time to time by adding a few drops of ether (Note 5). After the diazonium solution is added, the ice-bath is removed while stirring is continued at room temperature for half an hour.

The solution is then heated to boiling and carefully acidified to Congo Red with concentrated hydrochloric acid (sp. g. 1.19, about 600 cc.), which is added very slowly with constant stirring and scratching of the walls of the beaker. As the mixture becomes acid, the foam disappears and the thick precipitate of copper hydroxide is replaced by a granular one of crude diphenic acid. The beaker is then placed in running water until thoroughly cold; the crude diphenic acid is filtered by suction and washed with faintly acid, saturated ammonium chloride solution until free from copper salts, and then with water. If dried

at this point, the crude gray acid melts at 210–225° and weighs 65–83 g.

The crude diphenic acid is next transferred to a 1.5-l. flask and dissolved in 400–450 cc. of glacial acetic acid. Then 100 cc. of hot water is added and the dark solution boiled not more than ten minutes with 15–20 g. of zinc dust (Note 6). Towards the end of this treatment, 4 g. of decolorizing carbon (Norite) is added, and the solution is filtered hot through a large preheated Büchner funnel. The clear deep-red filtrate is heated to boiling in a 2-l. flask and 700–800 cc. of hot water added slowly with stirring so that no permanent precipitation occurs. The flask is then allowed to cool somewhat and crystallization started by vigorously scratching the inside of the vessel (Note 7). The mixture is allowed to stand at room temperature for at least four hours. The diphenic acid is then filtered with suction and washed with 100–200 cc. of water. The yield of acid melting at 226–228° is 40–50 g. (46–57 per cent of the theoretical amount).

## 2. Notes

1. The substitution of acetic for hydrochloric acid in the diazotization avoids the formation of *o*-chlorobenzoic acid and gives a crude product melting in some cases as high as 218–225°, as compared with 190–210° when hydrochloric acid is employed.

2. In almost all samples of commercial anthranilic acid, even though showing the correct melting point, a small amount of insoluble material remains on diazotization. The clear liquor should be removed from this by decantation.

3. Only a portion of the diazotized solution is placed in the separatory funnel, the remainder being kept in an ice-bath supplied as required.

4. The use of more than this quantity of ammonia leads to its reaction with the diazonium salt and the formation of a brown tar, in the presence of which the diphenic acid fails to precipitate in the acetic acid purification. Less than this amount leads to low yields. The quantity employed suffices to

neutralize the excess acetic acid in the diazonium solution and the diphenic acid formed and still have 2.5 moles in excess.

5. When commercial anthranilic acid is employed the foam is extremely troublesome. *n*-Butyl alcohol sometimes gives more satisfactory results than ether as an anti-foam agent.

6. The zinc-dust treatment serves to reduce and remove small amounts of azo compounds (notably *o*-azobenzoic acid) which always discolor the crude product. Attempts to purify the crude product by crystallization from 33 per cent alcohol invariably led to a darker colored product with the same melting point as the crude. The decolorizing carbon is not intended to decolorize the solution but to clarify the filtrate before the precipitation of the diphenic acid.

7. Diphenic acid solutions show a strong tendency to become supersaturated. Crystallization begins at once, however, on scratching the wall of the container and, when allowed to proceed slowly, leaves most of the colored impurities in the solution. If suddenly chilled out of the acetic acid, however, or if rapidly thrown out by reckless addition of acid in the initial precipitation, large amounts of tar and coloring matter will be carried down. The final product varies from very light gray to pure white.

### 3. Other Methods of Preparation

Diphenic acid was first prepared by oxidizing phenanthrenequinone with chromic acid.[1] Many later workers[2] have modified this process in minor details. Vorländer and Meyer[3] were the first to prepare diphenic acid from diazotized anthranilic acid and cuprous oxide, but their process is not well adapted to large scale preparation. Inasmuch as pure phenanthrene is now very difficult to obtain in quantity, the present process was devised for relatively large scale operation.

[1] Fittig and Ostermayer, Ann. **166**, 367 (1873).

[2] Fittig and Schmitz, *ibid.*, **193**, 116, (1878); Graebe and Aubin, *ibid.*, **247**, 263 (1888); Oyster and Adkins, J. Am. Chem. Soc. **43**, 209 (1921); Bischoff and Adkins, *ibid.*, **45**, 1031 (1923); Roberts and Johnson, *ibid.*, **47**, 1399 (1925).

[3] Ann. **320**, 138 (1902).

XII

## ETHYL BROMOMALONATE

$$CH_2(CO_2C_2H_5)_2 + Br_2 \rightarrow BrCH(CO_2C_2H_5)_2 + HBr$$

Submitted by C. S. PALMER and P. W. McWHERTER.
Checked by ROGER ADAMS and M. M. BRUBAKER.

### 1. Procedure

A 1-l. three-necked flask is fitted with a stirrer, a reflux condenser with a tube leading to a flask of water for absorption of hydrogen bromide, and a separatory funnel with a stem drawn to a fine tip which reaches almost to the blades of the stirrer. In the flask are placed 160 g. (1 mole) of ethyl malonate (Note 1) and 150 cc. of carbon tetrachloride. In the separatory funnel is placed 165 g. (1.03 moles) of dry bromine (Note 2). The stirrer is started, and a few cc. of bromine is run into the solution. A large electric bulb is held under the flask until the reaction starts. Then the rest of the bromine is added gradually at such a rate as to keep the liquid boiling gently. It is then refluxed until no more hydrogen bromide is evolved (about one hour). The mixture is cooled and washed five times with 50-cc. portions of 5 per cent sodium carbonate solution. It is then distilled under reduced pressure, fractions being taken up to 130°/40 mm. and at 130–150°/40 mm. The residue amounts to about 20 g. The lower boiling fraction is redistilled. The combined fractions boiling at 130–150°/40 mm. are redistilled under reduced pressure. The product boiling at 132–136°/33 mm. (121–125°/16 mm.) amounts to 175–180 g. (73–75 per cent of the theoretical amount). Redistillation of the low fractions gives about 15 g. more of the product.

## 2. Notes

1. Commercial ethyl malonate distilled under reduced pressure and collected over a 3° range was used.

2. Commercial bromine was dried by shaking with an equal volume of concentrated sulfuric acid. A slight excess of bromine is used to insure complete bromination.

## 3. Other Methods of Preparation

Ethyl bromomalonate is usually prepared without the use of a solvent.[1]

[1] Knoevenagel, Ber. **21**, 1356 (1888).

# XIII

## ETHYL *n*-BUTYLACETOACETATE

$$CH_3COCH_2CO_2C_2H_5 + C_2H_5ONa + CH_3(CH_2)_2CH_2Br \rightarrow$$
$$\underset{\textstyle (CH_2)_3CH_3}{CH_3CO\overset{}{C}HCO_2C_2H_5} + C_2H_5OH + NaBr$$

Submitted by C. S. Marvel and F. D. Hager.
Checked by Frank C. Whitmore and W. F. Singleton.

### 1. Procedure

A 5-l. round-bottom flask, fitted with an efficient mechanical stirrer (Note 1), a reflux condenser, the upper end of which is protected by a calcium chloride tube, and a separatory funnel, is arranged for heating on a steam bath.

In the flask is placed 2.5 l. of absolute alcohol (Note 2), and then there is added gradually 115 g. (5 moles) of metallic sodium cut into pieces. This requires three to four hours. After all the sodium has dissolved, 650 g. (5 moles) of ethyl acetoacetate (Note 3) is added. The stirrer is started and the solution heated to gentle boiling. To the boiling solution 750 g. (5.47 moles) of *n*-butyl bromide (Note 4) is added over a period of about two hours. The refluxing and stirring are continued until a sample of the solution is neutral to moist litmus paper. The time varies from six to ten hours.

When the reaction is complete, the mixture is cooled, and the solution is decanted from the sodium bromide. The salt is washed with 100 cc. of absolute alcohol, and the washings are added to the main solution. The alcohol (Note 5) is separated from the substituted acetoacetic ester by distilling through a short column from a steam bath. The crude residue after removal

of the alcohol weighs about 925 g. It is satisfactory for hydrolysis to give the corresponding ketone (p. 60). If the pure ester is desired, the crude product is distilled under reduced pressure. The yield of product boiling at 112–117°/16 mm. is 642–672 g. (69–72 per cent of the theoretical amount) (Note 6).

## 2. Notes

1. The stirrer should be efficient in order to prevent bumping due to the settling of the sodium bromide which is formed during the reaction.

2. The grade of absolute alcohol is important. Alcohol dried with sodium ethylate (Org. Syn. **5,** 56) is satisfactory. It is more effective to dry alcohol with magnesium methylate if the presence of methyl alcohol in the absolute alcohol is permissible. This may be done by dissolving 24 g. of magnesium turnings in 200 cc. of absolute methyl alcohol (the reaction is very vigorous) and then adding three liters of the ordinary grade of absolute alcohol (about 99.5 per cent). The mixture is refluxed for about five hours and distilled into the flask in which the absolute alcohol is to be used.

3. The ethyl acetoacetate used in these experiments boiled over a range of five degrees under reduced pressure. The product prepared as described in Org. Syn. **6,** 36, is satisfactory.

4. The *n*-butyl bromide (Org. Syn. **1,** 5) boiled over a range of three degrees. The excess was used in order to decrease the time necessary to complete the reaction.

5. The alcoholic solution should be protected from moisture and the alcohol which is recovered by the distillation treated with sodium and boiled under a reflux condenser to remove the excess of alkyl halide. After distillation the alcohol may then be used in a subsequent preparation.

6. This reaction is very general and other substituted acetoacetic esters may be obtained in approximately the same yields if this procedure is followed.

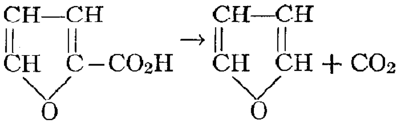
### 3. Other Methods of Preparation

Ethyl *n*-butylacetoacetate has always been prepared by the action of *n*-butyl bromide on the sodium salt of ethyl acetoacetate.[1] The procedure given above is the usual one for alkylating ethyl acetoacetate.

[1] Tafel and Jürgens, Ber. **42**, 2555 (1909); Shannon, Proc. Roy. Irish Acad. **36B**, 322 (1924) (C. A. **19**, 470 (1925) ); Hess and Bappert, Ann. **441**, 153 (1925).

## XIV

# FURAN



Submitted by W. C. Wilson.
Checked by Roger Adams and C. G. Gauerke.

### 1. Procedure

In a 200-cc. round-bottom flask is placed 80 g. (0.71 mole) of crude 2-furancarboxylic acid (Org. Syn. **6**, 44) (usually about 95 per cent pure). To the neck of the flask is fitted an upright tube 2.5 cm. in diameter and 15 cm. long, with a side arm of the same diameter leading out about 2 cm. from the top of the tube. This side arm is extended into the bottom of an efficient (25-cm.) soda-lime tower (Note 1) immersed in a water bath held at 40° to prevent condensation of the furan. From the top of the soda-lime tower an outlet tube (0.5 cm. in diameter) is extended to the top of an upright water condenser, to the lower end of which is attached a receiving flask surrounded by ice and salt (Note 2).

The top of the upright tube in the reaction flask is closed by a cork stopper holding a glass plunger which may be used for pushing back into the flask any sublimed 2-furancarboxylic acid.

The acid is heated just to its boiling point (200–205°) (Note 3), when it decomposes with the evolution of furan and carbon dioxide. The small amounts of 2-furan-carboxylic acid

that sublime are pushed back from time to time. The distillate is finally redistilled, when it is found to boil at 31–34° at 745 mm. The yield is 33–36 g. (72–78 per cent of the theoretical amount).

## 2. Notes

1. The drying column removes carbon dioxide, moisture, and some of the other by-products which are formed. The product which is collected is nearly pure, and the redistillation completes the purification.

2. In a number of experiments a second receiver was used in addition to the first one, but it was found that practically all of the furan condensed in the first receiver.

3. Care should be taken in heating 2-furancarboxylic acid. If the temperature is too low, decomposition takes place too slowly; if too high, much 2-furancarboxylic acid sublimes and causes difficulty. In one run a thermometer was placed in the melted acid. It read 200–205° during the evolution of the furan.

## 3. Other Methods of Preparation

Limpricht,[1] in 1873, prepared furan by heating barium 2-furancarboxylate with soda lime. It has since been prepared by the dry distillation of barium 2-furancarboxylate;[2] in small amounts by distillation of calcium succinate;[3] by the destructive distillation of resinous pine wood;[4] by heating succinaldehyde with water at 180°;[5] and by heating 2-furancarboxylic acid in a sealed tube.[2]

[1] Limpricht, Ann. **165**, 281 (1873).

[2] Freundler, Compt. rend. **124**, 1157 (1897); Bull. soc. chim. (3) **17**, 613 (1897).

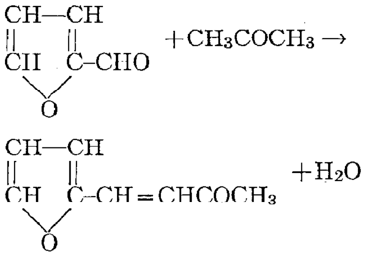
[3] Metzner and Vorländer, Ber. **31**, 1886 (1898).

[4] Atterberg, Ber. **13**, 879 (1880).

[5] Harries, Ber. **34**, 1496 (1901).

# XV

## FURFURALACETONE



Submitted by G. J. Leuck and L. Cejka.
Checked by Frank C. Whitmore and H. H. Rowley.

### 1. Procedure

In a 5-l. round-bottom flask equipped with a mechanical stirrer are mixed 385 g. (335 cc.) (3.8 moles) of 95 per cent furfural (Org. Syn. 1, 49) (Note 1) and 3 l. of water. Then 500 g. (630 cc.) (8.6 moles) of acetone is added. The mixture is stirred and cooled to 10° and to it is added 75 cc. of 33 per cent sodium hydroxide solution (Note 1), whereupon some heat is generated. Without cooling, the stirring is continued for four hours. At the end of this time 10 per cent sulfuric acid is added until the mixture is acid to litmus (about 350 cc.) (Note 2). The two layers which have formed are separated and the upper aqueous layer is distilled (Note 3) under ordinary pressure until the distillate no longer forms two layers. The bottom layer of this distillate is added to the original lower layer and distilled under reduced pressure from a 1-l. modified Claisen flask (Org. Syn. **1**, 40) provided with an air condenser and heated in an oil bath. The

receiving flask is placed in a large funnel connected with the drain. A stream of cold water is run over the receiver. When a solid appears in the receiver, distillation is interrupted, the liquid distillate is discarded, and the distillation is continued. The product which distils at 114–118°/10 mm. (135–145°/50 mm.) Note 4) weighs 310–340 g. (60–66 per cent of the theoretical amount, based on the furfural used). The yellow crystals melt at 37–39° and when melted show a sharp freezing point of 37° (Note 5).

## 2. Notes

1. Commercial chemicals were used. The use of purer chemicals, including furfural distilled over a 2° range under diminished pressure, gives no higher yield, but the product is lighter colored, although the boiling point and melting point are the same as with the crude materials.

2. When the alkali is neutralized, the mixture loses its milky appearance and forms definite layers.

3. The distillation of the water layer may be omitted, since it yields only 10–20 g. of the product.

4. A large residue of higher boiling material remains in the flask. This residue contains much difurfuralacetone, the formation of which takes place to a considerable extent in spite of the large excess of acetone used.

5. The highest melting point recorded in the literature is 39–40°. The crystals gradually become reddish on standing even in the dark. This change is much slower when freshly distilled furfural is used.

## 3. Other Methods of Preparation

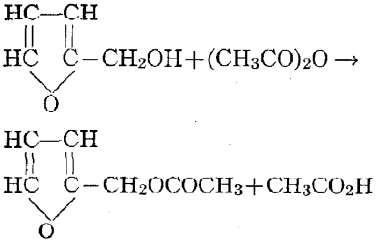
The method [1] of condensation of furfural with acetone in the presence of bases is the only one reported as giving furfuralacetone.

[1] Schmidt, Ber. **14,** 574, 1459 (1881); Claisen, Ber. **14**, 2468 (1881); Ann. **223,** 137 (1884).

XVI

## 2-FURYLMETHYL ACETATE

**(Furfuryl Acetate)**



Submitted by THE MINER LABORATORIES.
Checked by ROGER ADAMS and C. G. GAUERKE.

### 1. Procedure

A MIXTURE of 1 l. of benzene, 600 g. (6.1 moles) of 2-furylcarbinol (Org. Syn. **6**, 44) (Note 1), 225 g. of fused and powdered sodium acetate, and 650 g. (6.4 moles) of a good grade of acetic anhydride are placed in a 5-l. round-bottom flask (Note 2) fitted with a mechanical stirrer (Org. Syn. **1**, 4, Fig. 1*b*) and a reflux condenser provided with a calcium chloride tube. The flask is heated on a steam bath (Note 1) for four hours with stirring to prevent caking of the sodium acetate.

The reaction mixture is allowed to cool and is poured into 4 l. of cold water (Note 3). The upper layer is separated and allowed to stand for two hours over about 500 cc. of 5 per cent sodium carbonate solution with frequent shaking or mechanical stirring. This decomposes any excess of acetic anhydride. It

is finally washed with about 3 l. of water. The benzene solution is distilled under ordinary pressure to remove the benzene (800–900 cc. is recovered). The 2-furylmethyl acetate is distilled under diminished pressure, b.p. 69–70°/7 mm. The yield is 750–800 g. (87–93 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. If the water-insoluble form of the alcohol (Org. Syn. **6**, 46) is used, the mixture should be allowed to stand under a reflux condenser for about two hours before it is heated. During this period a certain amount of heat is evolved, and sometimes it is sufficient to cause the benzene to boil vigorously, thus making cooling necessary. After it has stood the required time, the mixture is refluxed as described above.

2. If a two- or three-necked flask is available it can be used to advantage.

3. The washing can best be done in a large separatory apparatus prepared by cutting the bottom out of an 18-l. (5-gal.) glass carboy and wiring into its neck a piece of glass tubing carrying a rubber tube and pinch clamp. The inverted carboy forms a useful separatory funnel of large capacity.

4. Saponification of the product with standard potassium hydroxide shows 93–94 per cent ester. It contains some furfuryl alcohol, the removal of which by fractional distillation is difficult, because the boiling points of the alcohol (169°/752 mm.) and the ester (175°/764 mm.) are so close together. Furfuryl acetate darkens on standing. It may be redistilled with little loss to give an almost colorless product.

## 3. Other Methods of Preparation

2-Furylmethyl acetate has been prepared by heating 2-furylcarbinol with acetic anhydride alone, or with acetic anhydride and sodium acetate.[1]

[1] Wissell and Tollens, Ann. **272**, 303 (1892); Zanetti, J. Am. Chem. Soc. **47**, 535 (1925).

XVII

## GUANIDINE NITRATE

$$NH_2C(NH)NHCN + NH_4NO_3 \rightarrow NH_2C(NH)NHC(NH)NH_2 \cdot HNO_3$$

$$NH_2C(NH)NHC(NH)NH_2 \cdot HNO_3 + NH_4NO_3 \rightarrow 2NH_2C(NH)NH_2 \cdot HNO_3$$

Submitted by TENNEY L. DAVIS.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

IN a 1-l. round-bottom flask is placed an intimate mixture of 210 g. of dicyanodiamide (2.5 moles) and 440 g. of ammonium nitrate (5.5 moles) (Note 1). The flask is introduced into an oil bath at 110–120° and the temperature of the oil is raised during about half an hour to 160°. The bath is then held at this temperature (Note 2) for three hours. During the first hour the mass melts to a clear liquid which begins to deposit crystals and finally sets to a solid cake (Note 3). At the end of three hours the flask is removed from the bath; the product is allowed to cool and is extracted on the steam bath with successive quantities of water (about 2 l. is necessary to bring all soluble material into solution) (Note 4). The solution is filtered to remove white amorphous insoluble material (ammeline and ammelide) (Note 5).

The filtrate contains guanidine nitrate along with a small amount of ammonium nitrate and very small amounts of dicyanodiamide and biguanide nitrate (Note 6). The solution is concentrated to about 1 l. and the guanidine nitrate which crystallizes on cooling is filtered off. A second crop is obtained by

concentrating to 250 cc. (Note 7). The combined yield of crude guanidine nitrate is 520–560 g. (85–92 per cent of the theoretical amount). The product may be purified by recrystallization from 1 l. of water (Note 8), taking a second crop after concentrating the mother liquor to 250 cc. The yield of recrystallized guanidine nitrate melting at 213–214° amounts to 500–520 g. (Note 9).

## 2. Notes

1. A 10 per cent excess of ammonium nitrate is used because the biguanide mononitrate which is formed as an intermediate is strongly basic and tends to attack the unreacted ammonium nitrate, as is evidenced by the liberation of ammonia during the heating. The excess of ammonium nitrate can be easily separated from the guanidine nitrate by the crystallization from water, and it does not interfere with the conversion of guanidine nitrate into nitroguanidine by the action of strong sulfuric acid.

2. When the molten mass reaches 160° its temperature begins to rise above that of the bath, generally reaching 200° during the course of five or six minutes. The mass should not be stirred at any time, especially before the mixture has completely melted; otherwise, the temperature may run somewhat higher.

3. The guanidine nitrate begins to crystallize soon after the temperature of the mixture begins to fall.

4. The hard cake goes into solution slowly and time must be given for each portion to become saturated before it is decanted.

5. When the hot filtrate cools, it will deposit flocks of ammelide along with the crystals of guanidine nitrate. Water may conveniently be added until the crystals dissolve, and the cold solution again filtered for the removal of ammelide.

6. This filtrate on evaporation to dryness and baking at 100° leaves a residue of 650 g., which is suitable for the preparation of nitroguanidine (p. 68).

7. At this point the mother liquor (about 200 cc.) may be discarded as it contains mainly ammonium nitrate.

8. Alcohol is a satisfactory solvent for guanidine nitrate but appears to have no advantage over water. A saturated solution of guanidine nitrate in water contains about 10 per cent at 15°.

9. The second mother liquor may advantageously be worked up with a subsequent run.

### 3. Other Methods of Preparation

Guanidine salts have been prepared by heating ammonium thiocyanate,[1] by hydrolysis of dicyanodiamide by acids,[2] (whereby one molecule of the guanidine salt is produced), and by the action of ammonium salts on dicyanodiamide,[3] from which two molecules of guanidine salt result. The nitrate has been prepared from the thiocyanate by the action of nitric acid.[4]

[1] Delitsch, J. prakt. Chem. (2) **8**, 240 (1873); (2) **9**, 2 (1874); Volhard, *ibid.* (2) **9**, 15 (1874).

[2] Baumann, Ber. **7**, 1766 (1874); Davis, J. Am. Chem. Soc. **43**, 669 (1921).

[3] Rathke, Ber. **18**, 3107 (1885); Davis, J. Am. Chem. Soc. **43**, 2234 (1921).

[4] Jousselin, Bull. soc. chim. (2) **34**, 497 (1880).

# XVIII

## HYDROGEN CYANIDE (ANHYDROUS)

$$NaCN + H_2SO_4 \rightarrow HCN + NaHSO_4$$

Submitted by K. ZIEGLER.
Checked by HENRY GILMAN and L. C. HECKERT.

### 1. Procedure

A 5-l. round-bottom flask, set up in a good hood (Note 1), is fitted with a three-holed rubber stopper that holds two 250-cc, separatory funnels, *A* and *B* (Fig. 1). A small funnel, *F*, (about 3–4 cm. in diameter) is suspended directly under the outlets of the two separatory funnels and is attached to the

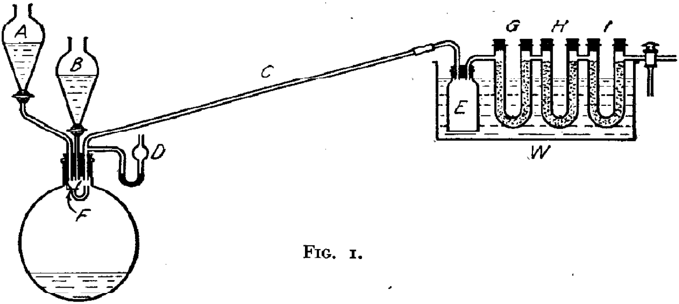



FIG. 1.

rubber stopper by a loop of stiff copper wire. The discharge tube of the funnel is bent in the shape of a U so that its end is about one cm. below the top of the funnel. In the third hole of the rubber stopper is inserted an inclined glass tube, *C*, of about 10 mm. internal bore and approximately 50 cm.

long. A mercury safety vent, *D*, is sealed in the side of this tube. *C* acts as an air condenser and leads to an empty gas bottle, *E*, of about 250 cc. capacity and then to three large U tubes, *G*, *H*, and *I*, filled with anhydrous calcium chloride. The gas bottle and the U tubes are contained in a water bath, *W*, warmed to 30–40°. The last calcium chloride tube is fitted with a three-way glass stopcock so that the gaseous anhydrous hydrogen cyanide may be used directly or diverted to an efficient condenser for liquefaction. The condenser is a glass coil of 4–5 mm. bore and about 50 cm. long that is surrounded by ice (Note 2) contained in a percolator arrangement like that described in Org. Syn. **6**, 13.

One of the separatory funnels is filled with 1 l. of sulfuric acid prepared by the careful addition of 392 g. (4 moles) (213 cc.) of concentrated sulfuric acid to 213 cc. of water. The other separatory funnel is filled with a solution of 203 g. of commercial sodium cyanide (about 96 per cent) (4 moles) dissolved in sufficient water to make 500 cc. of solution. Evolution of hydrogen cyanide takes place on the simultaneous addition of the two solutions. Practically all of the reaction occurs in the funnel, *F*, and the sodium bisulfate solution continuously drains into the flask so that fresh solutions are always present. The solution in the funnel remains clear as long as sufficient sulfuric acid is present. An excess of sodium cyanide colors the solution yellow and leads to the formation of a muddy brown precipitate. By adjusting the flow of solutions the rate of evolution is easily controlled, and the preparation requires no attention beyond that involved in the occasional replenishment of the solutions in the separatory funnels. The last part of the hydrogen cyanide can be driven from the apparatus by boiling the bisulfate solution for a few minutes. The yield of acid melting at −15° to −14.5° is 100–105 g. (93–97 per cent of the theoretical amount) (Notes 3 and 4).

## 2. Notes

1. Gattermann[1] recommends that the operator smoke during the preparation, for he found that a trace of hydrogen cyanide is

sufficient to give the tobacco smoke a highly characteristic flavor. This preliminary warning is useful in case of leaky apparatus or a faulty hood.

2. It is essential that the coil be cooled with ice only. A freezing mixture causes solidification of the hydrogen cyanide with consequent clogging of the apparatus.

3. The hydrogen cyanide is best kept over anhydrous calcium chloride. In this way it remains clear and water-white for months; otherwise, it soon becomes yellow, owing to the formation of azulmic acid.

4. If larger quantities of hydrogen cyanide are desired, the apparatus may be modified as suggested by Lindemann [3] by using a four-hole rubber stopper in the generating flask and fitting it with a siphon tube by means of which the sodium bisulfate solution can be removed from time to time. With this modification the generating flask need be of only 2- to 3-l. capacity.

## 3. Other Methods of Preparation

The only other method of preparative value for the generation of hydrogen cyanide is the reaction between potassium ferrocyanide and sulfuric acid.[1] It is convenient for the preparation of small amounts of hydrogen cyanide; however, it is too expensive in larger runs. The present method is based on the work of Ziegler [2] and Lindemann.[3]

[1] Gattermann, Ann. **357**, 318 (1907).

[2] Ziegler, Ber. **54**, 110 (1921).

[3] Lindemann, Ann. **431**, 291 (1923).

# XIX

## β-HYDROXYPROPIONIC ACID

### (Hydracrylic Acid)

$$CH_2OHCH_2CN + NaOH + H_2O \rightarrow CH_2OHCH_2CO_2Na + NH_3$$

$$2CH_2OHCH_2CO_2Na + H_2SO_4 \rightarrow 2CH_2OHCH_2CO_2H + Na_2SO_4$$

Submitted by R. R. READ.
Checked by H. T. CLARKE and C. R. NOLLER.

### 1. Procedure

To a cold solution of 160 g. (4 moles) of sodium hydroxide in 500 cc. of water in a 2-l. round-bottom flask provided with a mechanical stirrer is added slowly 250 g. (3.5 moles) of ethylene cyanohydrin (Org. Syn. **3**, 57), the temperature being kept below 30° (Note 1) by means of a cold water bath. The mixture is allowed to stand over night in the bath, when the flask is fitted with a two-holed rubber stopper bearing a capillary tube reaching almost to the bottom and a delivery tube bent slightly downward for attachment to a suction pump. The flask is then heated slowly to 80° during four hours by raising the temperature of the surrounding water. A rapid current of air is drawn through the mixture during the heating. The mixture is now evaporated to dryness under reduced pressure by heating in an oil bath, the temperature of which is raised as rapidly as the boiling of the material will permit. The oil bath is finally held at 125° until the product becomes pasty. The flask is allowed to cool, and 50 cc. of water is poured down one side of the flask, and the solid material at that point worked carefully into a paste with a stout stirring rod.

A cooled mixture of 200 g. (109 cc.) of concentrated sulfuric acid (2 moles) and 300 cc. of water is now added slowly with careful cooling (Note 2), the pasty mixture being stirred with a thermometer and the temperature not being allowed to rise above 35°. Sodium sulfate crystallizes during this addition. The mass is now shaken vigorously with 400 cc. of ether and allowed to stand for some minutes. The ether is then decanted as completely as possible and the residue filtered with suction. The sodium sulfate is now shaken with six successive 300-cc. portions of ether, the ether solutions being subsequently employed for extraction of the filtrate. This latter requires 10–14 such extractions (each with 300–400 cc. of ether) for the satisfactory extraction of the β-hydroxypropionic acid. The combined ethereal solution is dried over 50 g. of anhydrous sodium sulfate and the ether distilled from a water bath, the temperature of which is not allowed to rise above 50°. The product is then concentrated under reduced pressure from a water bath maintained at 55–60°. The residue should have attained constant weight after four to six hours of this treatment; it consists of a sirupy liquid of pale straw color which contains 75–80 per cent of β-hydroxypropionic acid (by titration) (Note 3). The yield is 120–125 g. (28–31 per cent of the theoretical amount).

## 2. Notes

1. If the temperature of the mixture of nitrile and sodium hydroxide is allowed to rise too soon or too rapidly, the evolution of ammonia may become almost explosive, as the reaction is exothermic.

2. The temperature during the addition of the sulfuric acid must be carefully controlled, as the heat of neutralization is sufficient to decompose the product. The use of a minimum amount of water is desirable in order to decrease the number of extractions.

3. β-Hydroxypropionic acid is an uncrystallizable and hygroscopic sirup. The 20–25 per cent of impurity remaining in the final product is largely water.

### 3. Other Methods of Preparation

β-Hydroxypropionic acid has generally been prepared by the hydrolysis of β-iodopropionic acid [1] or the corresponding bromo compound.[2] Owing to the readiness with which ethylene cyanohydrin may now be prepared, this was considered to be the most suitable starting product, alkali [3] being regarded as a more suitable hydrolytic agent than acid.[4] β-Hydroxypropionic acid has also been prepared by the action of alkali upon acrylic acid.[5]

[1] Beilstein, Ann. **122**, 369 (1862); Socoloff, Ann. **150**, 168 (1869); Heintz, Ann. **157**, 298 (1871); Wislicenus, Ann. **166**, 10 (1873).

[2] Lossen, Ann. **342**, 128 (1905).

[3] Wislicenus, Ann. **128**, 6 (1863).

[4] Erlenmeyer, Ann. **191**, 269 (1878).

[5] Erlenmeyer, Ann. **191**, 281 (1878); Linnemann, Ber. **8**, 1095 (1875).

XX

## p-IODOBENZOIC ACID

$$p\text{-}ClHgC_6H_4CO_2H + I_2 \rightarrow p\text{-}IC_6H_4CO_2H + HgClI$$

Submitted by FRANK C. WHITMORE and GLADYS E. WOODWARD.
Checked by HENRY GILMAN and C. C. VERNON.

### 1. Procedure

ONE hundred fifty grams (0.6 mole) of iodine is dissolved in 2.5 l. of 95 per cent ethyl alcohol in a 5-l. round-bottom flask set on a tripod and provided with a mechanical stirrer and a reflux condenser. To this solution is added 300 g. (0.84 mole) of powdered dry crude *p*-chloromercuribenzoic acid (Note 1) (p. 18). The mixture is stirred and heated. The acid gradually goes into solution and the color of iodine disappears. The hot stirred mixture is treated with iodine until a yellow color persists for at least ten minutes. This is conveniently done by weighing out iodine in 10-g. portions, dissolving in a little alcohol and adding through the condenser. The total amount of iodine required depends on the purity of the mercurated acid. It should not exceed 210 g. (0.83 mole). If there is any insoluble material left after an excess of iodine has been added, it is removed by rapid filtration through a pre-heated suction filter. On cooling, the filtrate yields about 175 g. of *p*-iodobenzoic acid. Concentration of the mother liquor yields crystals which are contaminated with mercuric iodide. The latter may be removed by grinding the crystals in a mortar with water and enough sodium iodide or potassium iodide to destroy the red color of the mercuric iodide (Note 2). The mixture is filtered and the crystals are washed with a little sodium iodide solution and

then with water. The washed *p*-iodobenzoic acid melts at 266–267°. The total yield is 150–170 g. (72–81 per cent of the theoretical amount).

## 2. Notes

1. The crude *p*-chloromercuribenzoic acid may be sucked as dry as possible and transferred in this pasty form to the iodine solution. If, however, it has caked at all, it must be thoroughly dried and powdered. A respirator should be worn as the dust is rather irritating.

2. Another method of removing most of the mercuric iodide is to grind the crystals, suspend them in a little water, and pour off the lighter suspension of iodobenzoic acid, leaving the heavy mercuric iodide behind. Washing with iodide solution is necessary to remove the last of the mercuric iodide.

## 3. Other Methods of Preparation

*p*-Iodobenzoic acid has been prepared by the oxidation of *p*-iodotoluene with chromic acid mixture[1] and with nitric acid;[2] from the nitrile obtained from *p*-iodonitrobenzene and potassium cyanide;[3] and from *p*-aminobenzoic acid by diazotization.[4]

[1] Körner, Z. Chem. **1868**, 327.
[2] Cohen and Raper, J. Chem. Soc. **85**, 1273 (1904).
[3] Richter, Ber. **4**, 553 (1871).
[4] Marshall, Ber. **28**, 338 (1895).

# METHYL *n*-AMYL KETONE

## (Heptanone-2)

$$\underset{\displaystyle |\atop (CH_2)_3CH_3}{CH_3COCHCO_2C_2H_5} + NaOH \rightarrow \underset{\displaystyle |\atop (CH_2)_3CH_3}{CH_3COCHCO_2Na} + C_2H_5OH$$

$$2\underset{\displaystyle |\atop (CH_2)_3CH_3}{CH_3COCHCO_2Na} + H_2SO_4 \rightarrow$$

$$2CH_3CO(CH_2)_4CH_3 + 2CO_2 + Na_2SO_4$$

Submitted by JOHN R. JOHNSON and F. D. HAGER.
Checked by FRANK C. WHITMORE and W. F. SINGLETON.

### 1. Procedure

In a 12-l. round-bottom flask, fitted with an efficient mechanical stirrer, is placed 5 l. of a 5 per cent solution of sodium hydroxide (6.25 moles). To this is added the crude ethyl *n*-butylacetoacetate (about 925 g.) (p. 36) obtained from 5 moles of ethyl acetoacetate. The mixture is stirred at room temperature for four hours, during which time the mono-substituted acetoacetic ester is completely saponified and passes into solution. The mixture is then allowed to stand until the unsaponified material separates completely as an oily layer. The aqueous layer is separated (Note 1) and transferred to a flask provided with a stopper fitted with a separatory funnel and a large bent glass tube leading to a condenser set for distillation.

Through the separatory funnel is added slowly 500 cc. of 50 per cent (sp. gr. 1.40) sulfuric acid (3.6 moles), which is somewhat more than the amount required to neutralize the alkali (6.25 moles) used in the saponification of the ester. When the evolution of carbon dioxide ceases to be vigorous, the reaction mixture is heated slowly to boiling, and from one-third

to one-half of the total volume is distilled. The distillate is make alkaline with solid sodium hydroxide (Note 2) and redistilled until 80–90 per cent has been collected.

In the distillate the ketone layer is separated from the water, and the latter is distilled until one-third has been collected. The ketone layer in this distillate is separated, and the water layer is again distilled. This procedure is repeated as long as any considerable amount of ketone is obtained in the distillate (Note 3). The combined ketone fraction is washed four times with one-third its volume of a concentrated solution of calcium chloride (sp. gr. 1.3 or greater) to remove alcohol (Note 4), then dried over 50 g. of solid calcium chloride, filtered and distilled. The yield of methyl *n*-amyl ketone boiling at 148–151° at 750 mm. is 300–350 g. (52–61 per cent of the theoretical amount, based upon the original ethyl acetoacetate) (Note 5).

## 2. Notes

1. The insoluble layer is usually quite small in amount and may be discarded. On distillation it yields but a small amount of ketone and monosubstituted ester, along with considerable high-boiling material, presumably the disubstituted ester, which was present in the crude ethyl *n*-butylacetoacetate.

2. The distillate is rendered alkaline to remove any acids formed by the acid decomposition of the substituted acetoacetic ester or unreacted ethyl acetoacetate.

3. With methyl *n*-amyl ketone this process was repeated three times after the first separation. In the case of higher ketones a fewer number of separations is required, while with the simpler ketones a greater number is advisable, on account of their solubility in water.

4. With the lower molecular weight ketones it is advantageous to distil the calcium chloride solution to recover the dissolved ketone. This is carried out exactly as described for the separation from the water. With methyl *n*-amyl ketone the loss is slight if a sufficiently concentrated solution of calcium chloride is employed.

5. Other ketones may be prepared by the same general procedure. Based upon the ethyl acetoacetate used, the following yields were obtained:

Methyl *n*-butyl ketone (hexanone-2) b.p. 126–128°, 50 per cent.
Methyl *iso*-butyl ketone (4-methylpentanone-2) b.p. 115–119°, 20 per cent.
Methyl *sec*-butylmethyl ketone (4-methylhexanone-2) b.p. 139–142°, 30 per cent.

The lower yields are due in some cases to the difficulty of isolating the products, and, in the last two, to the less complete reaction between the secondary alkyl bromide and the sodium derivative of ethyl acetoacetate.

### 3. Other Methods of Preparation

Methyl *n*-amyl ketone has been prepared by the hydration of heptine-1 and of heptine-2 under various conditions,[1] and by heating *n*-amyl propiolic acid with potassium hydroxide.[2] It has also been obtained by the oxidation of methyl *n*-amyl carbinol with chromic acid.[3]

The procedure used in the ketone decomposition of ethyl *n*-butylacetoacetate is adapted from that used by Michael and Wolgast [4] for ethyl ethylacetoacetate.

[1] Behal, Ann. chim. phys. (6 **15**, 270 (1888); Desgrez, *ibid.* (7) **3**, 228, 234 (1894).

[2] Moureu and Delange, Bull. soc. chim. (3) **29**, 674 (1903).

[3] Schorlemmer, Ann. **161**, 279 (1872).

[4] Ber. **42**, 3177 (1909).

## XXII

## α-METHYL MANNOSIDE

$$(C_6H_{10}O_5)n + nH_2O + nCH_3OH \rightarrow nCH_2OH(CHOH)_4\ CH(OH)OCH_3$$

Submitted by C. S. HUDSON.
Checked by FRANK C. WHITMORE and R. D. GREENE.

### 1. Procedure

ONE kilogram of dry finely ground vegetable ivory waste (Note 1) is added gradually to 1250 g. of 85 per cent sulfuric acid in an 8-l. (2-gal.) enamelled vessel (Note 2) at such a rate as to keep the temperature at 30–35° (one to two hours). The mass is well kneaded (Note 3) and then kept at about 25° for fifteen hours (Note 4). A mixture of 1 l. of acetone-free methyl alcohol and 250 cc. of pure concentrated hydrochloric acid (sp. gr. 1.19) (Note 8) is kneaded into the soft mass, which is then transferred to a 12-l. flask. The flask is adjusted on a large steam bath (Note 5), 6 l. of absolute methyl alcohol is added, and the mixture is refluxed eight hours. At the end of this time the mixture is cooled somewhat, and 100 g. of decolorizing carbon and 150 g. of infusorial earth or fuller's earth are added, and refluxing is resumed for half an hour. The solution is filtered hot with suction through a Büchner funnel previously heated by blowing steam into the side neck of the suction flask (Note 6). The cake is washed with 500 cc. of hot absolute methyl alcohol. The filtration is likely to be slow unless a large funnel (30 cm.) is used. The light yellow filtrate soon begins to deposit crystals (Note 7). It is kept in an ice box twenty

to fifty hours. The crystals are filtered off by suction, washed with 50 cc. of absolute methyl alcohol, then with 50 cc. of dry acetone, and dried on porous plates at room temperature. The yield is 480–520 g. The mannoside is pure enough for most chemical purposes. It melts at about 170° and has a rotation in water of +78.6°. If a purer product is desired, the mannoside may be crystallized from four parts of 80 per cent ethyl alcohol with 80–90 per cent recovery if the mother liquors are worked up. Slight acidity in the solutions used in recrystallization should be carefully neutralized with ammonia. The recrystallized mannoside melts at 188–189° and has a rotation of $[\alpha]_D^{20}$, +80.8°.

## 2. Notes

1. The ivory nut waste was obtained from the Rochester Button Company, Rochester, N. Y. It was ground in a mill, dried to constant weight at 100°, and sifted through a 20-mesh screen (8 per cm.).

2. The bottom of an Elyria enamelled kettle was used. A crock can be used almost as conveniently. On smaller runs a large porcelain mortar was used.

3. The kneading can conveniently be done by means of a heavy stick, the end of which has been thoroughly charred in a fire and then polished to remove loose carbon. Stirring is not practical.

4. A convenient method of heating is to suspend a 60-watt electric light about 20 cm. above the mixture.

5. The flask may be immersed half way in a large kettle of water heated on a large radial burner.

6. Another convenient device for rapid filtration is to use a large Witt plate in a steam funnel attached to a suction flask.

7. In some runs spontaneous crystallization is slow to start. It is advantageous to inoculate the solution with a crystal of the mannoside.

8. Later experiments indicate that the addition of hydrochloric acid is not essential since the sulfuric acid is sufficient to cause the formation of the mannoside. (C. S. Hudson.)

### 3. Other Methods of Preparation

α-Methyl mannoside has been prepared from mannose and methyl alcohol in the presence of hydrochloric acid.[1] The present method of preparing it directly from vegetable ivory has obvious advantages over any method for preparing it from isolated mannose.

[1] Fischer and Beensch, Ber. 29, 2928 (1896).

# XXIII

## NITROGUANIDINE

$$NH_2C(NH)NH_2 \cdot HNO_3 \rightarrow NH_2C(NH)NHNO_2 + H_2O$$

Submitted by Tenney L. Davis.
Checked by H. T. Clarke and Ross Phillips.

### 1. Procedure

To 500 cc. (Note 1) of concentrated sulfuric acid (sp. g. 1.84), previously cooled in a freezing mixture, is added in small portions and with hand stirring 560 g. of crude (Note 2) guanidine nitrate (obtained from 210 g. of dicyanodiamide as described on p. 46). The temperature is not allowed to rise above 20° during the addition. When all has been added, the milky mixture is allowed to stand at room temperature with occasional stirring until it is homogeneous and free from crystals (Note 3). It is then poured with stirring into 6 l. of a mixture of cracked ice and water. The precipitated nitroguanidine is filtered, washed free from acid, and recrystallized from the least possible amount (4–5 l.) of boiling water (Note 4). The yield (Note 5) is 380–390 g. (73–75 per cent of the theoretical amount, based on the dicyanodiamide used). The product melts with decomposition at about 232° (Note 6).

### 2. Notes

1. It has been found in checking that the use of 800 cc. of acid, while not necessary, gives a much less viscous solution, which becomes homogeneous more rapidly.

2. This contains ammonium nitrate, which, however, does not interfere with the reaction.

3. The mixture has to stand fifteen to twenty hours before solution is complete.

4. The solution should be allowed to cool slowly, preferably over night, when the nitroguanidine separates in long needles which resemble sublimed phthalic anhydride. The mother liquor contains only 3–4 g. per liter, and may be discarded.

5. In checking, yields amounting to 85–90 per cent of the theoretical quantity were obtained from pure guanidine nitrate.

6. Melting points varying between 220° and 250° have been obtained on the same sample, according to the rate of heating.

### 3. Other Methods of Preparation

Nitroguanidine may be prepared by the nitration of guanidine salts by means of nitric acid,[1] or by the action of concentrated sulfuric acid upon guanidine nitrate.[2] The nitration of guanidine thiocyanate yields a product which retains a small proportion of sulfur compounds, and the nitration of the sulfate requires vigorous treatment and gives poor yields. The present procedure, which yields the *alpha* form,[3] is simple and economical, and furnishes a good yield.

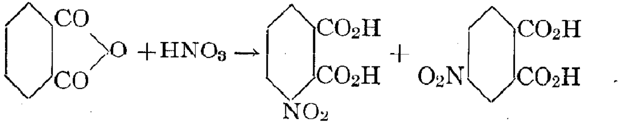
[1] Thiele, Ann. **270**, 16 (1892).

[2] Jousselin, Compt. rend. **88**, 1087 (1879); Pellizzari, Gazz. chim. ital. **21** (II), 406 (1891).

[3] Davis, J. Am. Chem. Soc. **47**, 1063 (1925).

# XXIV

## 3-NITROPHTHALIC ACID



Submitted by P. J. Culhane and Gladys E. Woodward.
Checked by Henry Gilman and C. C. Vernon.

### 1. Procedure

A 2-l. beaker placed on a piece of board in the bottom of a 4-l. (1-gal.) crock is fitted with a mechanical stirrer (Note 1). In the beaker are placed 650 cc. of commercial sulfuric acid (sp.g. 1.84) and 500 g. (3.4 moles) of technical phthalic anhydride. The mixture is stirred and steam is passed into the crock. When the mixture reaches 80°, the steam is shut off and 210 cc. of fuming nitric acid (sp.g. 1.51) is added slowly from a separatory funnel at such a rate as to maintain the temperature of the stirred mixture at 100–110°. The addition requires one to two hours. After the fuming acid has been added, 900 cc. of concentrated nitric acid (sp.g. 1.42) is added as rapidly as possible without causing the temperature to rise above 110° (Note 2). The mixture is then stirred and heated by passing steam into the crock for two hours longer. The mixture is allowed to stand over night and then poured into 1.5 l. of water in a 4-l. (1-gal.) crock. After cooling, the solid mixture of 3- and 4-nitrophthalic acids is filtered by suction through a Büchner funnel without a filter paper (Note 3) or through a filtros plate (Org. Syn, **5**, 7). The wet cake is returned to the

crock and stirred thoroughly with 200 cc. of water, which dissolves a large amount of the 4-nitrophthalic acid. The mixture is again filtered by suction (Note 4) and the wet cake is dissolved by boiling with 200–300 cc. of water (Note 5). The solution is filtered hot and stirred mechanically until crystallization starts. It is then allowed to stand over night, as the crystallization is slow. The crystals are filtered by suction and air-dried. The product melts at 205–210° in a sealed tube. The yield is 200–220 g. (28–31 per cent of the theoretical amount) (Note 6). Recrystallization of 200 g. of the crude acid from 300 cc. of water gives 170 g. of acid melting at 215–218° (capillary tube sealed 2 cm. from bottom). The washings and mother liquor from the crystallization may be saved for the recovery of 4-nitrophthalic acid (Note 7).

## 2. Notes

1. A large steam bath may be used instead of the crock. A motor should not be used directly above the nitration mixture because of the fumes evolved. The motor should be connected with the stirrer by a belt or, better still, a stirrer of the wind turbine type should be used. If a hood is not available, a 3-l. three-necked flask provided with a glass tube to conduct the fumes outside has been found satisfactory. When a beaker is used, it is recommended that two rectangular glass plates be placed across the top to reduce the danger of acid spattering.

2. The indicated proportions of fuming nitric acid and concentrated acid give as good results as fuming acid alone. The addition of the concentrated acid first does not work well.

3. The filtrate is repeatedly poured through the filter until clear. The mother liquor containing sulfuric acid and nitric acid cannot be worked up profitably for the recovery of the nitrophthalic acids.

4. The mother liquor is saved for the recovery of 4-nitrophthalic acid (Note 7). The product, if air-dried at this point, weighs about 500 g.

5. The amount of water needed depends on the dryness of the cake of crude acids.

6. By various refinements the yields may be increased, but the cost of the 3-nitrophthalic acid obtained is also increased. Because of the extreme cheapness of phthalic anhydride, it is inadvisable to increase the labor cost unduly in order to improve the yield. If a purer product is desired, crystallization from acetic acid will give 3-nitrophthalic acid melting at about 217° (closed tube).

7. The washings and mother liquors from crystallizations may be evaporated and esterified to separate the isomeric acids.[3]

About 370 g. of air-dried solid material may be recovered from the mother liquors and washings. Care must be exercised in concentrating these solutions, as the solid material chars readily when the solution becomes concentrated.

### 3. Other Methods of Preparation

3-Nitrophthalic acid has been prepared by the oxidation of nitronaphthalene,[1] and by the nitration of phthalic acid in a variety of ways by many different workers.[2] The present method is based on those of Bogert and Boroschek[3] and of Lawrance.[4]

[1] Beilstein and Kurbatow, Ann. **202**, 217 (1880); de Aguiar, Ber. **5**, 899 (1872).

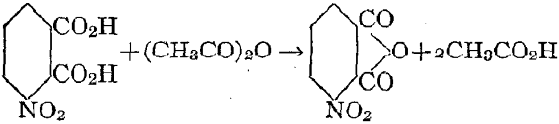
[2] Faust, Ann. **160**, 57 (1871); Miller, Ann. **208**, 223 (1881); Kenner and Mathews, J. Chem. Soc. **105**, 2476 (1914); Cohen, Woodroffe and Anderson, J. Chem. Soc. **109**, 232 (1916); Littmann, J. Am. Chem. Soc. **47**, 1980 (1925).

[3] J. Am. Chem. Soc. **23**, 743 (1901).

[4] J. Am. Chem. Soc. **42**, 1872 (1920).

XXV

## 3-NITROPHTHALIC ANHYDRIDE



Submitted by B. H. NICOLET and J. A. BENDER.
Checked by FRANK C. WHITMORE and W. F. SINGLETON.

### 1. Procedure

To 211 g. (1 mole) of 3-nitrophthalic acid (p. 70) in a 300-cc. round-bottom flask fitted with a reflux condenser is added 205 g. (2 moles) of acetic anhydride (99–100 per cent). The mixture is heated to gentle boiling until the acid is completely dissolved and then for about ten minutes longer. The hot mixture is poured (hood) into a 15-cm. porcelain dish and allowed to cool. The crystal mass is ground thoroughly in a mortar and filtered by suction. The crystals are returned to the mortar and the filtrate (about 140 cc.) is placed in a 300-cc. distilling flask. The crystals are ground with 150 cc. of alcohol-free ether (Note 1) and filtered. They are again returned to the mortar and similarly washed. After drying in the air for a short time, the product is dried to constant weight at 105°. The yield of product melting at 163–164° is 170–180 g. (88–93 per cent of the theoretical amount). The acetic acid filtrate is distilled with a thermometer in the liquid until the temperature is 150°. The distillate amounts to about 120 cc. The residue is poured into the mortar and, after cooling, is ground with some of the ether used in washing the original crystals. Thus about 10 g. of a product melting at 160–163° is obtained.

## 2. Note

1. Dry ether is recommended because ordinary ether contains alcohol, and the formation of some mono-ethyl ester may take place. Ordinary U.S.P. ether which has stood over calcium chloride for two days is satisfactory.

### 3. Other Methods of Preparation

3-Nitrophthalic anhydride has been prepared by heating the acid under various conditions [1] and by the action of acetic anhydride, [2] essentially as in the present method.

[1] Kahn, Ber. **35**, 3859 (1902).
[2] McKenzie, J. Chem. Soc. **79**, 1137 (1901).

## XXVI

## PENTENE-2

$$CH_3CH_2CH_2CHOHCH_3 \xrightarrow{H_2SO_4} CH_3CH_2CH{=}CHCH_3 + H_2O$$

Submitted by JAMES F. NORRIS.
Checked by FRANK C. WHITMORE.

### 1. Procedure

To a cooled mixture of 200 cc. of water and 200 cc. of concentrated sulphuric acid in a 1-l. round-bottom flask is added slowly 176 g. (2 moles, 214 cc.) of pentanol-2 (b.p. 118–120°) (Note 1). The flask is connected with a long efficient condenser for distillation (Note 2). The end of the condenser is provided with an adapter which passes well into a receiver surrounded by ice water (Note 2). The flask is heated on a boiling water bath as long as distillation takes place (two to three hours).

The distillate is shaken in the receiver with about 25 cc. of a 5 per cent solution of sodium hydroxide to remove any trace of sulfur dioxide that may be present. The hydrocarbon is separated and dried with 10 g. of anhydrous calcium chloride. It is then distilled, the fraction boiling at 35–41° (Note 3) being collected. The yield is 92–112 g. (65–80 per cent of the theoretical amount).

### 2. Notes

1. Pentanol-2 is now manufactured on a large scale from petroleum. As the quality of the commercial alcohol varies, the product should be distilled before use and the proper fraction

used. The material was kindly supplied by the Petroleum Chemical Corporation, Cambridge, Mass. (A. D. Little, Inc.).

2. Because of the volatility of the product, unusual precautions must be taken in its preparation to avoid loss.

3. Most of the product distils at 36–37°. The product may contain a small amount of the isomeric pentene-1. By redistilling it through a 25-cm. (10-in.) fractionating column containing small pieces of glass rod, the pure hydrocarbon can be readily obtained. Pentene-2 boils at 36.39°±0.04°/760 mm., melts at −138°±2° has the density $d_{4^\circ}^{15^\circ}$ 0.6555, and $n_D^{25}$ 1.3839.

## 3. Other Methods of Preparation

Pentene-2 has been prepared [1] by treating the iodide made from diethylcarbinol with alcoholic potash, by dehydrating active amyl alcohol by means of fused zinc chloride,[2] and from 3-bromopentane and alcoholic potash.[3]

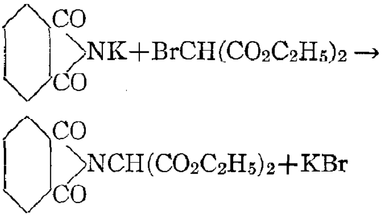
[1] Wagner and Saytzeff, Ann. **175**, 373 (1875).

[2] Tissier, Bull. soc. chim. (3) **9**, 100 (1893).

[3] Lucas and Moyse, J. Am. Chem. Soc. **47**, 1461 (1925).

## XXVII

## PHTHALIMIDOMALONIC ESTER



Submitted by A. E. Osterberg.
Checked by Frank C. Whitmore and H. C. Benedict, Jr.

### 1. Procedure

In a 600-cc. beaker 210 g. (0.87 mole) of ethyl bromomalonate (p. 34) (Note 1) and 165 g. (0.89 mole) of potassium phthalimide (p. 8) are intimately stirred together. The mixture is stirred approximately every ten minutes. If no spontaneous reaction starts in half an hour (Note 1), it is necessary to initiate the reaction by heating to 110–120°. The mixture then becomes liquid and can be stirred easily. It turns to a light brown color, especially near the top where it comes in contact with the air. When the temperature begins to drop, the mixture is heated in an oil bath at 110° for one hour to insure completion of the reaction. The mixture is then poured into a mortar where it solidifies to a solid mass (Note 2). When cold, the mixture is ground up with water and filtered to remove most of the potassium bromide. The precipitate is then reground with water and refiltered, finally washing the precipitate well with water. The solid material on the filter consists of some potassium bromide, some phthalimide, and the phthalimidomalonic ester.

Without drying, it is put into a 1-l. flask with 400 cc. of benzene and heated to boiling. After cooling, the insoluble bromide and phthalimide are removed by filtration. The filtrate contains some water, which is removed by means of a separatory funnel.

The benzene solution is dried with 20 g. of calcium chloride and the benzene removed by distillation under diminished pressure on a water bath. The residue is poured into a mortar where it solidifies. The crystalline mass is then ground with small amounts of ether (200 cc. in all), filtered, and washed with ether (about 100 cc.) until pure white. The yield of phthalimidomalonic ester melting at 73–74° is 155–162 g. From the ether filtrate after distilling the ether, there may be recovered a further amount by washing with a small amount of ether to remove the brown color. The total weight of ester obtained in the two crops is 180–190 g. (67–71 per cent of the theoretical amount).

## 2. Notes

1. When freshly prepared ethyl bromomalonate is used, the temperature of the mixture may rise spontaneously to 140°. In such event no heat should be applied until the temperature falls again.

2. If solidification does not take place as soon as the mixture is cold, about 100 cc. of water should be added. This accelerates the solidification.

## 3. Other Methods of Preparation

The present method is adapted from that of Sörenson.[1]

[1] Chem. Zentr. **1903**, II, 33.

# XXVIII

## TRIPHENYL STIBINE

$$C_6H_5Br + Mg \rightarrow C_6H_5MgBr$$

$$3C_6H_5MgBr + SbCl_3 \rightarrow (C_6H_5)_3Sb + 3MgBrCl$$

Submitted by G. S. HIERS.
Checked by HENRY GILMAN and F. SCHULZE.

### 1. Procedure

IN a 2-l. round-bottom three-necked flask fitted with a mercury-seal mechanical stirrer, a reflux condenser, and a separatory funnel is placed 40 g. (1.65 moles) of magnesium turnings (Note 1). This is covered with 200 cc. of dry ether, and there is then added 100 cc. of a mixture of 260 g. (1.65 moles) of dry bromobenzene and 800 cc. of dry ether. As soon as the reaction starts, 200 cc. more of dry ether is added and the remainder of the bromobenzene solution at such a rate as to cause gentle boiling (about two hours). With external cooling, the time may be shortened.

When all the bromobenzene has been added, there is added slowly through the separatory funnel a solution of 114 g. (0.5 mole) of freshly distilled antimony trichloride (m.p. 67–73°) in 300 cc. of dry ether. The reaction proceeds smoothly and even briskly with the freshly distilled chloride. However, if the latter has not been freshly prepared, gentle warming may be required to start the reaction. When all the antimony trichloride has been added (one to two hours), the mixture is heated on the steam bath for an hour longer.

When cool, the reaction mixture is poured slowly with stirring into 1 l. of ice and water (Note 2). If the stirring is thorough, most of the triphenyl stibine is to be found in the ether layer.

The hydrolysis mixture is filtered through a Büchner funnel and the residue on the filter extracted three times (Note 3) with 100-cc. portions of ether. The aqueous layer is separated and extracted twice with 200-cc. portions of ether. The combined ether portions are evaporated slowly on a steam bath to remove the ether, and there remains behind a yellow semi-solid which crystallizes to a white solid on cooling (Note 4). The yield of crude product melting at 49° is 145–160 g. (82–90 per cent of the theoretical amount). For purification from a small amount of diphenyl which is present in the crude product 90 g. of triphenyl stibine is dissolved in 200 cc. of petroleum ether (b.p. 40–50°) by warming on a steam bath. There is generally a small amount of insoluble residue which is filtered and the filtrate cooled in a freezing mixture. The triphenyl stibine separates as small prisms and weighs 58–65 g.; by further concentration of the filtrate to an approximate volume of 50 cc. and then cooling again, an additional 15–20 g. of product separates. Both portions melt at 50°.

## 2. Notes

1. The excess of the Grignard reagent insures the complete removal of all the halogen from the antimony.

2. During the hydrolysis the use of acids to dissolve the magnesium hydroxide must be avoided, for the presence of acid tends to decompose the antimony compound.

3. During the filtration some ether evaporates and the stibine compound is left on the filter with the magnesium hydroxide. Extraction is necessary to remove this product.

4. The same method may be used for the preparation of tri-*p*-tolyl-stibine. Starting with 282 g. of *p*-bromotoluene (Org. Syn. **5**, 21) and proceeding in the same manner as described there was secured 150–157 g. (77–80 per cent of the theoretical amount) of crude tri-*p*-tolyl-stibine. This product purified by recrystallization from methyl alcohol or ether melts at 125–126°. The reaction is somewhat more vigorous in this case and sometimes cooling is necessary at first.

### 3. Other Methods of Preparation

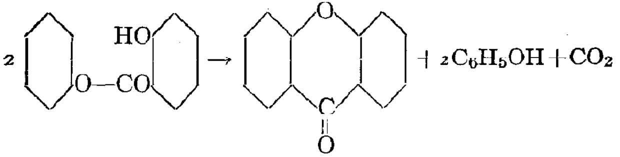
Triphenyl stibine has been prepared[1] from antimony trichloride and chlorobenzene dissolved in dry benzene in the presence of sodium. This yields triphenyl stibine dichloride, which on decomposition with hydrogen sulfide yields triphenyl stibine. Triphenyl stibine has also been prepared[2] by the action of phenyl magnesium bromide and antimony trichloride.

[1] Michaelis and Reese, Ann. **233**, 42 (1886).

[2] Pfeiffer and Heller, Ber. **37**, 4621 (1904).

# XXIX

## XANTHONE



Submitted by A. F. Holleman.
Checked by H. T. Clarke.

### 1. Procedure

Five hundred grams (2.34 moles) of phenyl salicylate is heated in a 1-l. special distilling flask having a wide (Note 1) side-arm 20–25 cm. long, and fitted with two thermometers, one extending to the bottom of the flask, and the other just below the side-arm. When the temperature of the liquid reaches 275–285°, phenol begins to distil. The heating is so regulated that the temperature of the vapor never exceeds 175° and preferably remains below 170° (Note 2). In this way the phenol distils at the rate of 5–10 drops per minute. The temperature of the liquid rises gradually (Note 3), and after six to seven hours reaches 350–355°. At this point the distillation of the phenol practically ceases; the weight of the distillate is 220–225 g.

The receiver is now changed, the lower thermometer is raised from the liquid (Note 4), and the contents of the flask distilled as rapidly as possible (Note 5). Heating is continued until the tarry residue begins to foam; towards the end of the distillation the color of the vapor becomes deep yellow with a greenish fluorescence. The distillate weighs 165–170 g.; it is poured

while still molten into a cold dish and allowed to cool, ground in a mortar with 100 cc. of 5 per cent sodium hydroxide, and warmed on the steam bath for ten to fifteen minutes with 400 cc. of this solution. When cold, the xanthone is filtered off, washed free of alkali, and dried. A small amount of low-melting impurity is removed by boiling for ten to fifteen minutes with 250 cc. of methyl alcohol, cooling, filtering, and washing with the same solvent. A few grams can be recovered from the filtrate. The product melting at 170–172°, after softening slightly at 168–170°, weighs 141–145 g. (61–63 per cent of the theoretical amount). It is pure enough for the preparation of xanthydrol (p. 88). A purer product may be obtained by recrystallization from twenty parts of 95 per cent ethyl alcohol, from which it separates as pale yellow needles, melting at 173–174.°

## 2. Notes

1. The side-arm should have an internal diameter of at least 10 mm. in order to minimize the danger of stoppage by solidified distillate. This danger occurs particularly when the higher melting xanthone first begins to distil. No condenser is employed, the flask used as a receiver being cooled sufficiently by the air to condense all the vapors.

2. The regulation of temperature is difficult at first, but becomes easier after the first half-hour.

3. In consequence of this gradual rise in temperature, it is necessary to increase the size of the flame gradually.

4. Although the boiling point of xanthone is about 350°, the liquid in the flask reaches temperatures which would be dangerous to a mercury thermometer.

5. If a Pyrex flask is used, it is not only safe, but advisable, to remove the wire gauze and heat directly with the free flame. This permits the xanthone to be distilled rapidly and with a minimum loss.

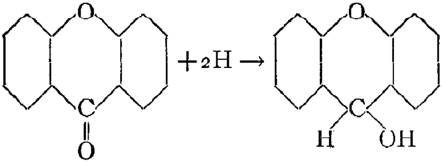
### 3. Other Methods of Preparation

The procedure is based on the directions of Graebe,[1] which outline the most convenient method of preparing xanthone. Somewhat similar is that of Perkin,[2] in which salicylic acid is first converted by boiling with acetic anhydride into salicylide, which on distillation is partially converted into xanthone. A practically quantitative yield of xanthone is stated to be obtainable by warming *o*-phenoxybenzoic acid with concentrated sulfuric acid,[3] but the preparation of this intermediate product is less satisfactory.

[1] Ann. **254**, 279 (1889).
[2] Ber. **16**, 339 (1883).
[3] Graebe, Ber. **21**, 501 (1888).

# XXX

## XANTHYDROL



Submitted by A. F. Holleman.
Checked by H. T. Clarke and C. R. Noller.

### 1. Procedure

An amalgam prepared from 9.0 g. (0.39 mole) of sodium and 750 g. (55 cc.) of mercury (Note 1) is warmed to about 50° (Note 2) in a 500-cc. Pyrex round-bottom flask (Note 3). To it is then added a cold suspension of 25 g. (0.13 mole) of xanthone (p. 84) in 175 cc. of 95 per cent ethyl alcohol. The flask is at once stoppered, held in a cloth, and vigorously shaken, raising the stopper from time to time to release any pressure. The temperature rises rapidly to 60–70°. The solid xanthone rapidly goes into solution, a very faint and transient blue color being developed. At the end of about five minutes the alcoholic solution is clear and practically colorless. After shaking for ten minutes longer, the mercury is separated and washed with 10–15 cc. of alcohol. The alcoholic solution is filtered while warm and slowly poured with stirring into 2 l. of cold distilled water. The precipitated xanthydrol is filtered with suction, washed with water until free of alkali, and dried at 40–50° to constant weight. The crystalline product, which weighs 23–24 g. (91–95 per cent of the theoretical amount), melts at 121–123° and is practically pure (Note 4).

## 2. Notes

1. The amalgam may be conveniently prepared by placing the sodium in the 500-cc. flask, covering it with 15–20 cc. of dry toluene and cautiously melting the metal over a free flame. The flame is then extinguished and the mercury added in drops, with occasional shaking. The reaction is extremely vigorous at first, but the rate of addition may be rapidly increased after the first 2–3 cc. of mercury has been added. The addition is so regulated that the toluene boils continuously, and it is finally allowed to volatilize completely. The toluene vapor remaining above the amalgam tends to protect it from the action of the air.

2. The amalgam is semi-solid at room temperature, but is completely melted at 50°. If made as in Note 1, it is merely allowed to cool to 50° before adding the alcoholic xanthone.

3. A thick-walled flask is necessary; although no great pressure is developed at any time, the impact of the mercury during shaking might break thin glass.

4. Xanthydrol is employed as a reagent for the determination of urea, with which it forms an insoluble condensation product. The material obtained is entirely satisfactory for this purpose; if desired, however, it may be recrystallized from alcohol, whereupon the melting point is raised by about 1°.

## 3. Other Methods of Preparation

Xanthydrol was first prepared by reducing xanthone by means of zinc dust in the presence of boiling alcoholic sodium hydroxide;[1] it was later shown by Fosse that it could be conveniently prepared by the action of a low percentage sodium amalgam upon xanthone in alcohol. The method is based upon the directions of Fosse.[2]

[1] Meyer and Saul, Ber. **26**, 1276 (1893); Adrian, Rec. trav. chim. **35**, 180 (1915).

[2] Ann. chim. (9) **6**, 58 (1916).

# ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers following the name of a compound refer to the volume and page of "Organic Syntheses.")

Allyl alcohol (**1**, 15), see **6**, 103

Benzoin (**1**, 33), see **6**, 103

*n*-Butyl *n*-butyrate (**5**, 23). If after the addition of the *n*-butyl alcohol, the oxidation mixture is heated on the steam bath to 90–100° until the supernatant liquid is practically colorless and then the reaction mixture is worked up as described, the yield of ester is increased to 147–149 g. (64–65 per cent of the theoretical amount).

If the ratios of the starting materials are changed slightly the yield of ester is further increased. Thus when 148 g. (2 moles) of *n*-butyl alcohol, 187 g. (0.62 mole) of crystallized sodium dichromate and 500 g. (5.1 moles) of sulfuric acid (sp. g. 1.84) are used and the reaction mixture heated after the addition of the butyl alcohol the yield of ester is 57–61 g. (70–75 per cent of the theoretical amount). (Private communication from W. J. Hickinbottom.) (Compare also Reilly and Hickinbottom, Scientific Proceedings of the Royal Dublin Society, **16**, 246 (1921).)

Cyclohexyl carbinol (**6**, 22). The amount of cyclohexyl bromide indicated in line 6 should be 163 g. (1 mole).

9, 10-Dibromoanthracene (**3**, 41), see **6**, 103

2-Furancarboxylic acid (**6**, 44) is most satisfactorily purified by recrystallizing from carbon tetrachloride. A few cc. of water should be added to coagulate and float the dark impurities. The clear subjacent liquid is separated and deposits colorless crystals of correct melting point.

Furfural (**1**, 49), see **6**, 103.

Methylene iodide (**1**, 5[illegible]). The methylene iodide obtained after vacuum distillation melts at 6°.

Pinacol hydrate (**5**, 87). The mixture should be chilled and kept cold for several hours instead of a few minutes.

# AUTHOR INDEX

(This index comprises names from all volumes of this series. The numbers after each name refer to a volume and page in "Organic Syntheses.")

# SUBJECT INDEX

*(This Index Comprises Material from all Volumes of this Series.)*

(Names of compounds in small capital letters indicate substances for which directions are given, the numbers in bold face type refer to volumes of Organic Syntheses, numbers in italics refer to pages in those volumes on which preparative directions are given, and numbers in Arabic refer to pages on which the compounds or subjects are mentioned in connection with other preparations. For example: ACETOACETIC ESTER, **4**, 45; **6**, *36* indicates that acetoacetic ester is mentioned in volume 4 on page 45 and that directions for its preparation are given in detail in volume 6 on page 36; Acetophenone, **2**, 1 indicates that this substance is mentioned in volume 2 on page 1 but that no directions for its preparation are given in this series.)

## C

## T

# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS



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VOL. VIII


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# PREFACE TO VOLUME VIII

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THE general plan of Organic Syntheses has been discussed in the prefaces of the previous volumes. In this volume are published two distinctly different methods of preparation for each of two compounds. The directions for producing β-chloropropionic acid first from acrolein and second from trimethylene chlorohydrin, and for producing trimethylacetic acid first from *tert*-butyl chloride and second from pinacolone, have been included. This has been deemed advisable since in some countries one raw material is more readily available than the other.

As the size of each volume must be limited there will necessarily be a delay in the publication of the directions submitted by contributors. Moreover, in certain instances, attempts by the editors to check the preparations have not met with immediate success. It is hoped, however, that former as well as new contributors will send in any preparations which may seem suitable for these publications.

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# ORGANIC SYNTHESES

## I

## ACETAMIDINE HYDROCHLORIDE

$$CH_3CN + C_2H_5OH + HCl \rightarrow CH_3C\begin{array}{l}\diagup OC_2H_5\\ =NH\cdot HCl\end{array}$$

$$CH_3C\begin{array}{l}\diagup OC_2H_5\\ =NH\cdot HCl\end{array} + NH_3 \rightarrow CH_3C\begin{array}{l}\diagup NH_2\cdot HCl\\ =NH\end{array} + C_2H_5OH$$

Submitted by A. W. Dox.
Checked by Frank C. Whitmore.

### 1. Procedure

Dry hydrogen chloride (Org. Syn. **2**, 30) (Note 1) is passed into a solution of 100 g. (2.44 moles) of thoroughly dry acetonitrile (Note 2) in 113 g. of absolute ethyl alcohol (Note 1) contained in a 1-l. weighed suction flask (Note 3) surrounded by a freezing mixture of ice and salt, until an increase in weight of 95 g. (2.6 moles) is obtained. This requires about four hours (Note 4) but the time is diminished considerably if proper mechanical stirring is used. The flask is now tightly stoppered, the side arm being attached to a calcium chloride tube, and allowed to stand until the mixture has set to a solid mass of crystals. Usually this requires two or three days.

A solution of dry ammonia gas in absolute ethyl alcohol is prepared and titrated against standard hydrochloric acid, using methyl orange as the indicator. The solution should contain at least 9 per cent of ammonia by weight (Note 5).

The solid crystalline mass of acetimido ethyl ether hydrochloride is broken up and transferred to a dry mortar in which

it is ground to a paste with 100 cc. of absolute alcohol and returned to the flask (Note 6). It is then stirred mechanically with an excess of the alcoholic ammonia solution (500 cc. of 9 per cent solution or an equivalent amount of a more concentrated solution). The crystals gradually dissolve and ammonium chloride separates. After stirring for three hours the ammonium chloride is filtered by suction and the filtrate evaporated on the steam bath to a volume of about 200 cc. when a considerable quantity of crystals separates. On cooling, the acetamidine hydrochloride separates in long colorless prisms. These are filtered by suction, washed with 10 cc. of cold alcohol, and dried in a desiccator over sulfuric acid. Concentration of the mother liquor gives a second crop. The product melts at 164–166° and is readily soluble in alcohol and in water. The yield varies from 185–210 g. (80–91 per cent of the theoretical amount). The product is somewhat deliquescent and should be kept in a tightly stoppered bottle.

## 2. Notes

1. The dryness of the reagents affects the yield seriously because of the ease with which the intermediate imido ether is hydrolyzed. The hydrogen chloride must be thoroughly dried by passing it through two wash bottles containing sulfuric acid. If the wash bottles are not effective, a tube containing glass beads mixed with phosphorus pentoxide should be used after the wash bottles. It is well to protect the side arm of the flask by means of a calcium chloride tube. The absolute alcohol used should be at least 99.5 per cent (Org. Syn. 5, 56).

2. If commercial acetonitrile is used directly, the yields are poor. It should be dried over calcium chloride for at least a week, filtered, and distilled, the fraction boiling at 76–81° being used.

3. If a thinner flask is used, there is danger of its being cracked during the experiment.

4. If a proper safety bottle is placed between the drying train and the flask of acetonitrile, the treatment with hydrogen chloride does not require constant attention during this time.

5. When weaker solutions of ammonia were used, the yields were lower.

6. The grinding of the imido ether hydrochloride is very important, as lumps of this material become coated with ammonium chloride, which prevents the complete action of the ammonia.

## 3. Methods of Preparation

The only practical method of preparation is that of Pinner,[1] on which the present directions are based.

[1] Pinner, Ber. **16**, 1654 (1883); **17**, 178 (1884).

## II

# ALLYL CYANIDE

$$2CuSO_4 + 4NaCN \rightarrow 2CuCN + (CN)_2 + 2Na_2SO_4$$
$$CH_2{=}CHCH_2Br + CuCN \rightarrow CH_2{=}CHCH_2CN + CuBr$$

Submitted by J. V. SUPNIEWSKI and P. L. SALZBERG.
Checked by FRANK C. WHITMORE,
H. F. HERZOG, and GLADYS E. WOODWARD.

## 1. Procedure

A. *Preparation of Cuprous Cyanide.* (Note 1)—In a 6-l. round-bottom flask fitted with a stopper carrying a mechanical stirrer, a separatory funnel, and a gas exit tube leading to a good hood (Note 2), is placed a solution of 650 g. (2.6 moles) of crystallized copper sulfate in 4 l. of water. The flask is surrounded by an oil bath and heated to about 80°. The stirrer is started and a solution of 255 g. (5.2 moles) of sodium cyanide (Note 3) in 650 cc. of water is added from the separatory funnel over a period of about one-half hour. Then the mixture is boiled until no more cyanogen gas is evolved. This requires about five to ten minutes.

The cuprous cyanide, which begins to separate as a light tan precipitate as soon as any of the cyanide solution is added, is allowed to settle and the solution is decanted. The precipitate is filtered, then washed with water (1 l.) and finally with alcohol (500 cc.) and ether (300 cc.). After drying at 110° for about thirty-six hours, the product weighs 200–210 g. (85–90 per cent of the theoretical amount).

B. *Preparation of Allyl Cyanide.*—In a 1-l. round-bottom flask fitted with a condenser (Note 4) and a mechanical stirrer are placed 220 g. (1.83 moles) of allyl bromide (Note 5) and 170 g.

(1.9 moles) of dry cuprous cyanide (Note 6). The mixture is heated in a water bath and the stirrer rotated slowly by hand until the reaction starts (about fifteen to thirty minutes). When the reaction once begins, it becomes vigorous, and the heating bath must be replaced by a cooling mixture of ice and water in order to avoid loss of product through the condenser. After the vigorous reaction has subsided, the water bath is replaced, the mechanical stirrer is started and the mixture is heated until no more allyl bromide refluxes. This requires about one hour.

The condenser is then set for distillation and the allyl cyanide is distilled from the flask by heating it in an oil bath with stirring (Notes 7 and 8). Upon redistillation the allyl cyanide is pure and boils at 116–121° with almost no loss. The yield is 98–103 g. (80–84 per cent of the theoretical amount).

## 2. Notes

1. Technical cuprous cyanide dried at 110° gives as good results as the specially prepared substance.

2. The cyanogen evolved in this reaction should be led into a flue with good suction draft. It may be burned if a trap is placed in the system to allow the moisture to condense.

3. The ordinary technical sodium cyanide is used.

4. A very efficient condenser is needed as the mixture refluxes vigorously during the first part of the reaction. A condenser of the bulb type about 90 cm. long is satisfactory. If a less efficient condenser is used, the upper end should be fitted with a tube leading into an empty flask to catch any material forced out.

5. The allyl bromide (Org. Syn. 1, 3) should be dried over calcium chloride, filtered and redistilled, the fraction boiling at 69–71° being used.

6. The cuprous cyanide must be dry, as small amounts of moisture reduce the yield considerably (about 15 per cent). With some samples of technical cuprous cyanide a larger amount must be used.

7. Toward the end of this distillation it is advisable to connect with the suction to remove the last of the allyl cyanide from the solid residue in the flask.

8. The residue in the flask is very tarry. It is best removed by careful treatment with strong nitric acid, then with water, and finally with hot alcohol. If necessary, the treatment is repeated several times.

### 3. Methods of Preparation

Allyl cyanide has been found in oil of mustard [1] and has been prepared from allyl chloride and potassium cyanide,[2] allyl bromide and potassium cyanide,[3] allyl iodide and potassium cyanide[4] and silver cyanide.[5] The method described in the procedure is essentially that of Bruylants, who has shown that the yields are much better when dry cuprous cyanide is treated with allyl bromide.[6]

[1] Will and Körner, Ann. **125**, 273 (1863).

[2] Pinner, Ber. **12**, 2053 (1879).

[3] Pomeranz, Ann. **351**, 357 (1907); Lespieau, Compt. rend. **137**, 262 (1903); Lespieau, Bull. soc. chim. (3) **33**, 58 (1905).

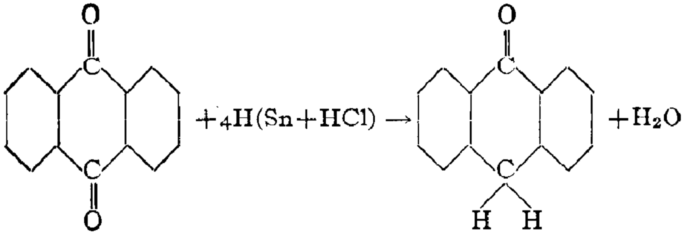
[4] Rinne and Tollens, Ann. **159**, 106 (1871).

[5] Lieke, Ann. **112**, 317 (1859).

[6] Bruylants, Bull. soc. chim. Belg. **31**, 175 (1922).

## III

## ANTHRONE



Submitted by KURT H. MEYER.
Checked by J. B. CONANT and W. C. BOYD.

### 1. Procedure

IN a 2-l. round-bottom flask fitted with a reflux condenser, 105 g. (0.5 mole) of anthraquinone, m.p. 276–280° (corr.), is mixed with 100 g. (0.86 mole) of granulated tin, and 750 cc. of glacial acetic acid is added. The contents of the flask are heated to boiling, and in the course of two hours, 250 cc. of c.p. hydrochloric acid (sp. gr. 1.19) is added in 10 cc. portions to the boiling mixture. At the end of this time all of the anthraquinone should have gone into solution; if not, more tin and hydrochloric acid are added.

The liquid is filtered with suction through a Gooch crucible with a fixed porous plate (Note 1), and 100 cc. of water is added. The anthrone crystallizes at about 10°. After being dried on a porous plate, it melts at about 153° (corr.). The yield is 80 g. (82.5 per cent of the theoretical amount). On recrystallization from a 3 : 1 mixture (Note 2) of benzene and petroleum ether about 60 g. of anthrone melting at 154–155° (corr.) is obtained (62 per cent of the theoretical amount).

## 2. Notes

1. The liquid can also be filtered through a fluted filter paper, but this is slower.

2. The proportions do not make much difference as far as the yield is concerned, but the substance is more soluble in mixtures rich in benzene. About 10–12 cc. of the 3 : 1 mixture is required for each gram of anthrone. The anthrone may be more readily dissolved if it is added to the estimated quantity of hot benzene on the steam bath, and the petroleum ether is then added. About two-thirds of the mother liquor may be distilled off through a condenser and used in later runs. The residual mother liquor deposits about 12 g. of rather impure anthrone.

## 3. Methods of Preparation

Anthrone has been prepared by the reduction of anthraquinone with tin and hydrochloric acid,[1] and with aluminium bronze.[2]

[1] Meyer, Ann. **379**, 55 (1911).
[2] Eckert and Pollak, Monatsh. **38**, 12 (1917).

IV

# APPARATUS FOR CATALYTIC REDUCTION

Submitted by ROGER ADAMS and V. VOORHEES.
Checked by HENRY GILMAN and S. A. HARRIS.

## 1. Procedure

I. *The Apparatus* (Fig. 1). A Prest-o-lite tank A from which the filling has been removed (Note 1), or any other similar tank of about 8–10 l. capacity, may be conveniently used as a container for hydrogen. The top of the tank contains two openings B and C. In B is welded a tube holding a gauge and valve, and through this tube the hydrogen from a large cylinder D is introduced into the tank. In C is welded another tube controlled by a needle valve. E is used for the vacuum, a manometer G being introduced into this system, and F for a tube leading to the reaction bottle H. These outlets are so arranged that it is possible to shut off the tank from either outlet and also to make a direct connection between the vacuum and the bottle H, leaving tank A out of the circuit. The connection between the tank A and the bottle H is a heavy taped rubber tube (Note 2) which is in turn connected to a glass tube inserted through the stopper of the bottle. The rubber tube and stopper should be high-grade and must be carefully boiled with alkali before being used (Note 3). The arrangement for shaking the bottle is shown in the diagram (Note 4). The driving pulley is connected to the reaction bottle by a wooden or preferably a metal rod. The rod in turn is attached by a yoke to a metal ring which circles the bottom of the bottle. The ring opens on the back side of the bottle and is held together by a wing-nut and bolt. In order to hold the stopper in the

bottle when the latter is filled with hydrogen under pressure, a metal strip I is clamped tightly over the stopper. This strip is screwed to the long wooden bottle holder which extends between the bearings, and a short wooden piece which fits

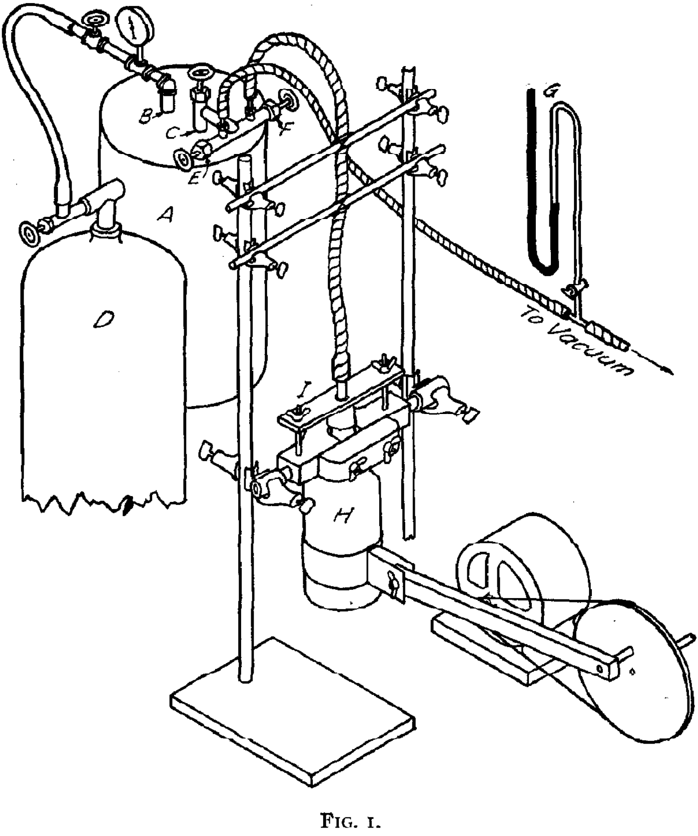



FIG. 1.

around the neck of the bottle is attached to the longer one by means of screws held by wing-nuts. This arrangement permits removal of the bottle from the apparatus without detaching the metal strip.

The chief precautions in setting up this reduction outfit are

first, to have every piece free from catalytic poisons and second, to be certain that there are no leaks (Note 5). The latter are sometimes an annoying factor and the complete apparatus should be carefully tested before attempting any reductions for standardizing the hydrogen tank. The apparatus is put together in final form with the empty reduction bottle attached to the hydrogen tank exactly as it is arranged in a reduction. The tank is then filled with hydrogen until the gauge reads 2.5–3 atm. (40–45 lbs.) and the temperature of the tank recorded. The reading of the gauge is observed as soon as equilibrium is reached and the bottle is then shaken for six to eight hours. Observations are made of the drop in pressure, taking into account any change of temperature which may occur during this time. In general if the drop in pressure is less than 0.03 atm. (0.5 lb.) in the time indicated the apparatus may be considered sufficiently free from leaks for ordinary work.

For some reactions it is advantageous to heat the mixture, and the following arrangement is very satisfactory for this purpose. The bottle H is wrapped with moistened asbestos paper to a thickness of about 3 mm. and the paper is then allowed to dry. When the asbestos is thoroughly dry the bottle is wound with a coil of No. 24 Nichrome wire, beginning the coil at the bottom of the bottle and making the turns about 9 mm. apart. The wire is then covered with a 3 mm. layer of asbestos, which is moistened and allowed to dry, after which the wire is wound around the bottle in another coil from top to bottom. The second coil is covered with asbestos as before, and the ends of the wire are connected to the terminal wires from a source of current. These wires are led along the bottle to the neck and held by means of tape in order to avoid excessive shaking. A variable resistance in the circuit is used to regulate the temperature.

II. *Use of the Apparatus.*—The tank A is filled with hydrogen to a pressure of 3–3.5 atm. from the cylinder D (Note 6). The solution, in a suitable solvent, of the substance to be reduced is poured into the bottle H and the platinum oxide (p. 92) is added (Note 7). The bottle is attached to the apparatus and evacu-

ated by opening valves E and F and closing C. In the case of low-boiling solvents, the evacuation is continued only until the solvent begins to boil; in other cases it is continued until the pressure as recorded by the manometer remains fairly constant. The valve E is then closed and hydrogen is admitted to the bottle H from the tank A by opening valve C (Notes 8 and 9). When the pressure in the bottle has become adjusted the pressure of the hydrogen and the temperature of the tank A are recorded. Shaking is started. Within a few minutes the brown platinum oxide turns black (see Note 5, p. 95) and the absorption of hydrogen begins. The shaking is continued until the theoretical amount of hydrogen has been absorbed. The hydrogen remaining in the bottle is removed, air is admitted and the mixture allowed to stand or, if necessary, shaken for a few minutes in order to aid the settling of the catalyst. In certain cases where the catalyst settles spontaneously at the end of the reduction it is not necessary to shake the mixture with air. The solution may be decanted from the main portion of the catalyst and a second reduction carried out. In cases where the catalyst cannot be used directly for another reduction (see Note 8, p. 97) the solution is filtered, preferably through an asbestos filter (Note 10) and fresh solvent is used for washing. The reduction product is isolated from the filtrate, usually by distilling off the solvent. The reduction of ethyl *p*-nitrobenzoate to ethyl *p*-aminobenzoate (p. 66) and benzalacetophenone to benzylacetophenone (p. 36) are described in detail in this volume.

III. *Standardization of the Apparatus.*—After making certain that there are no leaks in the apparatus (Note 5) the hydrogen tank may be standardized by reducing 11.6 g. (0.1 mole) of pure maleic acid (Note 11) dissolved in 150 cc. of 95 per cent alcohol using 0.1 g. of catalyst (p. 92). The reduction is carried out according to the procedure described in part II. Shaking of the mixture is continued until no more hydrogen is absorbed; the theoretical amount is absorbed by 0.1 mole of maleic acid within twenty or thirty minutes. The temperature of the tank is recorded. The decrease in pressure corresponds to 0.1 mole of hydrogen at the observed temperature. If the succinic acid

is desired it may be recovered merely by filtering the platinum, evaporating the alcohol and crystallizing from about 10–15 cc. of boiling water. The yield of product is 10–11.5 g. (84–98 per cent of the theoretical amount) depending on the care used in crystallization.

## 2. Notes

1. The bottom of the tank is cut off, the filling removed, and the bottom welded on again.

2. A copper tube may be used for this connection but is less satisfactory since the shaking tends to wear it out at the joints.

3. It is advisable to boil the tube and stopper with several portions of 20 per cent sodium hydroxide until the solution is no longer colored yellow, after which the boiling is carried out several times with distilled water.

4. The motor, pulley and the supports for the reaction vessel must be attached firmly to a heavy wooden stand which will allow as little motion as possible in the apparatus during shaking, thus reducing to a minimum the possibility of the gradual formation of leaks.

The arrangement for shaking should be so made that the reaction bottle is agitated at a rate above which no difference in the speed of reduction is observed. In this laboratory the motor used is a 1/30 h.p., 1760 r.p.m., the pulley on the motor 2.5 cm. in radius, and the wooden driving pulley 7.5 cm. in radius. The distance from the center of the pulley to the hole for attaching the rod to the reaction bottle is 3.2 cm., the distance from the center of the pulley on the motor to the center of the driving pulley to the bottle attachment is 30 cm. Considerable latitude is possible in these measurements. Although the apparatus in Fig. 1 is readily set up in any laboratory, a more compact and more stable form is shown in Fig. 2. The uprights which support the bottle consist of 1.3 cm. (one-half inch) piping surmounted by T-couplings. The uprights, driving pulley, and motor are firmly screwed down to a heavy wooden stand. An apparatus similar to this can be purchased complete from the Standard Calorimeter Co., East Moline, Ill.

5. It is quite necessary that the welding of the tank is perfect and free from pin holes. Leaks frequently appear where the tubes are welded in the top of the tank. These may be eliminated by brazing the joints. A less satisfactory way is to use a cement of litharge and glycerol. This cement may also be used with success on leaky valves. Occasionally leaks occur in the rubber tubing or its connections with the bottle or tank, but these are unusual.

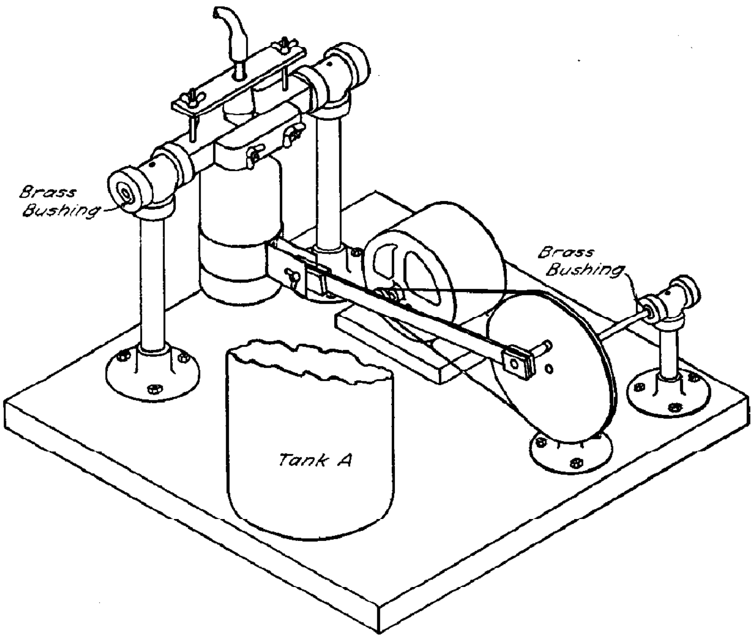



FIG. 2.

6. Electrolytic hydrogen was used in all experiments. This hydrogen is essentially free from all impurities except oxygen. Since oxygen in general has no harmful effect upon the reduction, no purification is necessary. If, however, oxygen-free hydrogen is needed, it must be passed over heated platinized asbestos.

7. This procedure may be varied in certain cases where it seems advantageous to reduce the platinum oxide to platinum black in the presence of the solvent alone (see Note 12, p. 98).

8. During the reductions it is usually advisable not to allow the pressure in the tank A to drop below about 2 atm. if the reduction is to be carried out in minimum time. When the gauge registers 2 atm. the tank is closed off from the reducing bottle and the pressure is increased to about 3–3.5 atm. by the admission of more hydrogen from D.

9. Ordinarily traces of air in the hydrogen have no deleterious effect upon the reductions. If in any experiment, absolute freedom from air is desired the bottle may be evacuated and refilled with hydrogen two or more times. In this way the air is all washed out of the bottle.

10. When paper filters are used the rapid suction of air through the paper in the presence of the catalyst often causes spontaneous combustion of the filter. Paper filters may be used, however, if care is taken to keep the filter covered with solvent while suction is being applied; just before the last portion of solvent has run through, the suction is stopped.

11. Instead of pure maleic acid, 10.6 g. (0.1 mole) of pure benzaldehyde may be used for the standardization. In this case 1 cc. of 0.1 molar ferrous sulfate is added to the mixture of benzaldehyde, alcohol and catalyst before the reduction is started (see Note 13, p. 98). The reduction is complete in fifteen to thirty minutes.

## 3. Forms of Apparatus

Other forms of catalytic reduction apparatus which may be used in the laboratory have been described in the following articles.[1]

[1] Paal and Amberger, Ber. **38**, 1390 (1905); Paal and Gerum, Ber. **41**, 813 (1908); Waser, Ueber Derivate des Cyclooctans (Promotionsarbeit) Zürich, 1911, p. 54; Willstätter and Hatt, Ber. **45**, 1472 (1912); Skita and Meyer, Ber. **45**, 3594 (1912); Stark, Ber. **46**, 2335 (1913); Boeseken, Van der Weide and Mom, Rec. trav. chim. **35**, 267 (1916); Rosenmund and Zetzsche, Ber. **51**, 580 (1918); Adams and Voorhees, J. Am. Chem. Soc. **44**, 1403 (1922); Klimont, Chem. Ztg. **46**, 275 (1922); Escourrou, Parfums France **2**

V

# *l*-ARABINOSE

## Hydrolysis of Mesquite Gum

Submitted by ERNEST ANDERSON and LILA SANDS.
Checked by H. T. CLARKE and H. J. BEAN.

### 1. Procedure

FIVE hundred grams of mesquite gum (Note 1) is dissolved (Note 2) in 3 l. of cold water in a 5-l. round-bottom flask; a cold solution of 125 g. of concentrated sulfuric acid in 80 cc. of water is added and the mixture warmed at 80° for six hours (Note 3) in a large water bath. The acid is neutralized by gradual addition of 140 g. of powdered calcium carbonate (Note 4), and the solution with excess calcium carbonate is heated in a boiling water bath for an hour to complete the neutralization. The calcium sulfate is filtered off and washed with about 2 l. of hot water. The filtrate is concentrated in an evaporating dish (Note 5) on the boiling water bath to a volume of 650–700 cc.

The solution is transferred to a 3-l. flask, using about 50 cc. of water for rinsing, and to it is added, with violent (Note 6) shaking, twice its volume (1400–1500 cc.) of 95 per cent ethyl alcohol. The solution is decanted from the gummy residue and the latter extracted three times with methyl alcohol under reflux, each time with 500 cc. of the solvent. In order to remove all the arabinose from the salts the precipitate is dissolved in 200–220 cc. of water, transferred to an evaporating dish, and 400 cc. of 95 per cent ethyl alcohol is stirred in with a heavy rod. The clear alcohol solution is decanted and the solid triturated twice with 300 cc. portions of methyl alcohol.

All the alcoholic extracts (both ethyl and methyl) are combined, shaken thoroughly, and 95 per cent ethyl alcohol added as long as any appreciable precipitate forms (Note 7). The solution is allowed to stand for some hours until it is clear, decanted, and concentrated in vacuo on a boiling water bath to a thin syrup (Note 8). Crystallization usually begins as soon as the syrup is cool though it is sometimes necessary to seed with arabinose.

After crystallization has begun 100 cc. of 95 per cent ethyl alcohol is stirred in, taking care not to precipitate any appreciable amount of gum. Crystallization is allowed to become complete in a cool place, occasionally stirring with a heavy rod. After about two days the crystalline arabinose is filtered off and washed with 200 cc. of 95 per cent ethyl alcohol. To secure further crops of arabinose from the mother liquor and washings, the solvent is distilled off under reduced pressure on the boiling water bath, and the residual gum dissolved in 200 cc. of hot methyl alcohol (Note 9). The solution is cooled, seeded with arabinose if necessary, set in the refrigerator for at least one day and the arabinose filtered off. After the first two crops of crystals have been secured, the organic salts that originally dissolved along with the arabinose begin to interfere with the crystallization. To remove these, the solvent is distilled off in vacuo on the boiling water bath, the residue dissolved in approximately 200 cc. of boiling methyl alcohol and 95 per cent ethyl alcohol added slowly with shaking until no more precipitate forms (about 40 cc. is necessary). The solution is allowed to cool and is decanted from the gummy salts; the solvent is then distilled from the sugar on the steam bath, finally under reduced pressure. The sugar is dissolved in a minimum volume of hot methyl alcohol, cooled, seeded with arabinose if necessary, set in the refrigerator to crystallize and the arabinose filtered off. If an appreciable amount of mother liquor is obtained, a fourth crop of crystals can be secured without again removing the gummy salts. In this way a total yield of 180–230 g. of crude arabinose can be obtained from the gum. The first two crops of crystals are easily obtained and amount

to approximately 90 per cent of the total yield. The melting point of the crude sugar varies from 147 to 152°.

The crude powdered sugar is purified by heating 200 g. of it for forty-five minutes on the boiling water bath with 300 g. of glacial acetic acid,[1] allowing to cool, filtering off the arabinose, washing it with 500 cc. of 95 per cent ethyl alcohol in four portions, and drying at 50–60°. It then weighs about 182 g. and melts at 155–157°. It may be recrystallized from five times its weight of 76 per cent ethyl alcohol, with the use of 10 g. of decolorizing charcoal, Norite. The yield is about 127 g. and the melting point is 155–157°; the crystals are now perfectly colorless.

## 2. Notes

1. Mesquite gum is collected by the natives in the southwestern United States and northern Mexico. It is carried by most drug stores in this region and may be purchased from the Martin Drug Company of Tucson, Arizona.

2. If the mixture of mesquite gum and water is allowed to stand for ten hours with frequent shaking it will form a clear solution. If the mixture of gum and water is heated in the boiling water for an hour with frequent stirring the gum will also dissolve but the resulting solution is turbid.

3. Most of the arabinose is liberated during the first three hours' heating. The longer heating is necessary only in case the highest yield of arabinose is desired or the salts are to be used later for the preparation of galactose. No galactose is liberated by heating to 80° for six hours. However, some of this sugar is produced at 100° and seriously interferes with crystallization of the arabinose.

4. The solution is apt to foam over during neutralization. This may be prevented by adding to the foaming solution from time to time small amounts of *n*-butyl alcohol to break up the bubbles.

5. The solution may foam so badly that it is difficult to distil off the water under reduced pressure. In checking, it has

been found possible to do so if as much as 200–300 cc. of butyl alcohol has been added during neutralization.

6. If the mixture is merely gently shaken at this point much arabinose is contained with the precipitate, and the yield falls to as low as 30 per cent. of the amount obtained otherwise.

7. Appreciable amounts of organic salts dissolve during the extraction of the sugar and interfere seriously with the crystallization of the latter. Most of the salts are precipitated by addition of 95 per cent ethyl alcohol, leaving the sugar in solution.

8. If all the water is removed at this stage by heating the gum in vacuo for some time, the sugar will not crystallize readily.

9. Methyl alcohol, purified by distillation over quicklime, is the most satisfactory solvent for use in crystallizing the arabinose from the gummy mixture; ethyl alcohol at this stage usually causes the precipitation of a gum.

### 3. Methods of Preparation

The preparation of arabinose from various plant products has been repeatedly described in the literature. The most important sources are cherry gum,[2] beet pulp,[3] and as has recently been shown by the present authors,[4] mesquite gum. The chief advantages of the preparation from mesquite gum are that the material is readily available in large amounts, the process is simple, and the yield comparatively large. The present procedure is a modification of the original method of Anderson and Sands.

[1] Hudson and Dale, J. Am. Chem. Soc. **39**, 322 (1917).

[2] Bauer, J. prakt. Chem. **34**, 46 (1886); Kiliani, Ber. **19**, 3029 (1886); cf. Browne, Handbook of Sugar Analysis, 548 (John Wiley, 1912).

[3] Gaertner, Z. Ver. deut. Zuckerind. **1919**, 232 [C. A. **14**, 1455 (1920)]; Harding, Sugar **24**, 656 (1922) [C. A. **17**, 1164 (1923)].

[4] Anderson and Sands, Ind. Eng. Chem. **17**, 1257 (1925).

# VI

## BENZALANILINE

$$C_6H_5CHO + C_6H_5NH_2 \rightarrow C_6H_5CH{=}NC_6H_5 + H_2O$$

Submitted by Lucius A. Bigelow and Harry Eatnough.
Checked by Henry Gilman and J. D. Robinson.

### 1. Procedure

In a 500-cc. three-neck, round-bottom flask provided with a mechanical stirrer is placed 106 g. (1 mole) of benzaldehyde (Note 1), and 93 g. (1 mole) of aniline is added with rapid stirring. After a few seconds a reaction occurs with evolution of heat and separation of water. The mixture is allowed to stand fifteen minutes and is then poured, with vigorous stirring, into 165 cc. of 95 per cent alcohol in a 600-cc. beaker. Crystallization begins in about five minutes, and the mixture is allowed to stand, first ten minutes at room temperature, and then thirty minutes in ice water. The almost solid mass is next transferred to a large Büchner funnel, filtered by suction, pressed out, and air dried. The yield of pure benzalaniline melting at 52° is 152–158 g. (84–87 per cent of the theoretical amount).

By concentrating the mother liquor to about half of its original volume at room temperature or lower, under reduced pressure by means of a water pump, an additional 10 g. of benzalaniline may be obtained. This is of good quality and melts at 51° (Note 2).

### 2. Notes

1. Freshly distilled reagents must be used to obtain the yields described. Distillation through a column is recom-

mended. The benzaldehyde should be washed with 5 per cent sodium carbonate solution before being vacuum distilled.

2. Removal of the alcohol by distillation at ordinary pressure gives a much darker product.

### 3. Methods of Preparation

These are discussed in Org. Syn. 5, 13. The present method is simpler than that described there, and although the yields are approximately alike in the two methods, the product obtained here is purer. Excluding the drying of the crystals, the entire procedure may be completed in about two hours.

Benzalaniline has also been prepared by the condensation of aniline and benzaldehyde in dilute alcohol saturated with carbon dioxide.[1]

[1] Pyl, Ber. 60, 287 (1927).

# VII

# BENZOHYDROL

$$C_6H_5COC_6H_5 + 2H(Zn+NaOH) \rightarrow C_6H_5CHOHC_6H_5$$

Submitted by C. S. Marvel and N. A. Hansen.
Checked by J. B. Conant and G. M. Bramann.

## 1. Procedure

In a 3-l. three-neck, round-bottom flask fitted with a mechanical stirrer and a reflux condenser with a wide inner tube, are placed a solution of 200 g. (5 moles) of pure sodium hydroxide in 2 l. of 95 per cent alcohol (Note 1) and 200 g. (1.1 moles) of benzophenone (p. 26). The stirrer is started and the solution is heated to boiling until it has turned dark brown (about twenty minutes) (Note 2). To this brown solution 200 g. (about 2.6–3 moles) of technical zinc dust (about 85 per cent pure) is added over a period of twenty minutes. The solution is heated and stirred after all of the zinc has been added until the brown color has disappeared (usually about one hour). The hot solution is filtered and the residue is washed twice with a little hot alcohol (100 cc.). The filtrate is poured into five volumes of ice water acidified with about 425 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The benzohydrol separates as a white crystalline mass and is filtered by suction. The yield of crude air dried product melting at 65° is 192–200 g. (95–99 per cent of the theoretical amount). From 200 g. of crude product in 200 cc. of hot alcohol there is obtained, after cooling in an ice-salt mixture, filtering and drying, 140–145 g. of product melting at 68°. The benzohydrol remaining in the mother liquors may be precipitated with water.

## 2. Notes

1. The directions in the literature usually call for the use of absolute alcohol and potassium hydroxide. The water present in ordinary alcohol does not interfere and sodium hydroxide can be substituted for potassium hydroxide. The alcoholic alkali is most easily prepared by dissolving the sodium hydroxide in 100 cc. of water and then adding 1900 cc. of absolute alcohol.

2. Unless the benzophenone is heated with the alcoholic alkali until a brown color is produced it is impossible to get a reduction. Several runs were made in which the alkali was dissolved in the hot alcohol, the benzophenone put in and the zinc dust added immediately in portions. No reduction took place.

## 3. Methods of Preparation

Benzohydrol has been obtained by reducing benzophenone with sodium amalgam,[1] with metallic calcium and alcohol,[2] with hydrogen in the presence of a catalyst,[3] with zinc, aluminium or sodium in strongly alkaline solutions,[4] with zinc dust and alcoholic potassium hydroxide solution,[5] and electrolytically.[6]

[1] Linnemann, Ann. **125**, 230 (1863); **133**, 6 (1865).

[2] Marschalk, Ber. **43**, 642 (1910).

[3] Vavon, Compt. rend. **155**, 287 (1912).

[4] Böeseken and Cohen, Verhandel Akad. Wetenschappen Amsterdam, **16**, 91 (1913) [Chem. Zentr. **1915** (1), 1375.]

[5] Montagne, Rec. trav. chim. **25**, 402 (1906).

[6] Müller, Z. Electrochem. **16**, 240 (1910).

VIII

## BENZOPHENONE

$$2C_6H_6 + CCl_4(+AlCl_3) \rightarrow C_6H_5CCl_2C_6H_5 + 2HCl$$

$$C_6H_5CCl_2C_6H_5 + H_2O \rightarrow C_6H_5COC_6H_5 + 2HCl$$

Submitted by C. S. Marvel and W. N. Sperry.
Checked by J. B. Conant and G. M. Bramann.

### 1. Procedure

In a 5-l. two-neck, round-bottom flask fitted with a good mechanical stirrer (Note 1), a separatory funnel, a thermometer, and a reflux condenser connected with a trap (Note 2) for absorbing the hydrogen chloride evolved, are placed 455 g. (3.4 moles) of anhydrous aluminium chloride (Note 3) and 1 l. (10.2 moles) of dry carbon tetrachloride (Note 4). The flask is surrounded by an ice bath (Note 5). The stirrer is started and when the temperature of the carbon tetrachloride has dropped to 10–15°, 50 cc. of dry thiophene-free benzene (Note 6) is added all at once. The reaction begins immediately as is indicated by the evolution of hydrogen chloride and a rising temperature. As soon as the reaction has started, salt is added to the ice in the cooling bath in order to get more effective cooling. When the temperature begins to fall after the reaction has started, a mixture of 550 cc. (a total of 6.7 moles) of thiophene-free benzene and 550 cc. (a total of 14.5 moles) of carbon tetrachloride is run in at such a rate that the temperature is kept between 5° and 10° (Note 4). If efficient cooling is maintained, this addition requires one to two hours. The stirring is continued for about three hours after the benzene-carbon tetrachloride solution has been added, while the temperature is held at about 10°. The stirring is then discontinued and the mixture is

allowed to stand about twelve hours. During this time the mixture comes to room temperature. The stirrer is then again started and about 500 cc. of water is slowly added. External cooling is used in order that the water may be added more rapidly. The excess carbon tetrachloride usually refluxes during this part of the procedure. The reaction mixture is then first heated on a steam bath to remove most of the excess of carbon tetrachloride, then the mixture is distilled with steam to carry over the remaining carbon tetrachloride (Note 7), and to hydrolyze the benzophenone dichloride to benzophenone. The carbon tetrachloride comes over in about thirty minutes but the steam distillation is continued for about one hour to insure complete hydrolysis. The upper benzophenone layer is then separated from the aqueous layer and the latter is extracted with about 200 cc. of benzene. The benzene solution and the benzophenone are transferred to a 1-l. modified Claisen flask (Org. Syn. **1**, 40) for distillation. The benzene and any water that is present are removed under ordinary pressure and the benzophenone is distilled under reduced pressure (Note 8). The yield is 490–550 g. (80–89 per cent of the theoretical amount based on the benzene) of a product boiling at 187–190°/15 mm., and solidifying to a white solid melting at 47–48°. The material sometimes has a bluish tinge. This may be removed by moistening with benzene and centrifuging.

## 2. Notes

1. The stirrer should be very efficient as otherwise the aluminium chloride tends to cake on the sides of the flask. This makes cooling very difficult and thus increases the time necessary for the addition of the benzene-carbon tetrachloride mixture.

2. A convenient trap (Fig. 3) devised by John R. Johnson for the absorption of hydrogen chloride, or for the elimination of sulfur dioxide, hydrogen cyanide, etc., may be arranged as shown in the figure. The gases are led into a chamber in which a stream of water (from the reflux condenser in this case) flows downward into a large bottle. The bottle is provided with a

bent tube which serves as a siphon drain. The gases are thus brought into contact with a flowing stream of water so that the heat of solution is dissipated, and the level of the water in the lower bottle serves as a seal to prevent escape of the gases into the atmosphere. Water-insoluble gases are drawn out through the siphon drain directly into the sink.

If the gas chamber is of sufficient capacity there is practically no danger of water being drawn back into the reaction vessel.

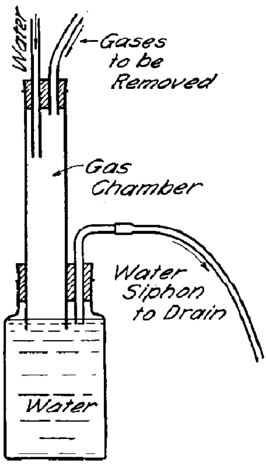



FIG. 3.

but care should be exercised when the reaction flask is cooled. For the reaction described here, a gas chamber about 2.5 cm. in diameter and 20–25 cm. in length was found to be satisfactory.

3. A good grade of technical anhydrous aluminium chloride was used to obtain the results given in the procedure. The yield falls off considerably when the quality of this reagent is not good.

4. No difference in yield is noticed in using the ordinary "pure" grade of carbon tetrachloride and the sulfur-free C.P. grade. It is easily dried by distilling the commercial product and rejecting the first 10 per cent of the distillate.

5. It is necessary to allow the reaction to start before packing in an ice-salt mixture. If the temperature is too low (below 10°) the reaction does not start. After the reaction has started, the cooling should be as efficient as possible so that the mixture of benzene and carbon tetrachloride may be added in the minimum amount of time. If the temperature drops below 5° the reaction is too slow. If the temperature goes above 10° there is increasing formation of tarry matter and lowering of the yield.

6. The yield is 5 to 10 per cent lower if the ordinary technical grade of benzene is used. The benzene is dried in the same manner as the carbon tetrachloride (Note 4).

7. About 1050–1150 cc. of carbon tetrachloride is recovered. This contains a small amount of benzene. However, it may be used in a succeeding run if it is dried over calcium chloride and distilled. No difference in the yield is noticed when recovered carbon tetrachloride is used.

8. There is considerable tendency for the benzophenone to foam over during the early part of the vacuum distillation and care must be taken to prevent this.

### 3. Methods of Preparation

Benzophenone has been prepared by the distillation of calcium benzoate,[1] by the action of benzoyl chloride on benzene in the presence of aluminium chloride,[2] by the action of phosgene on benzene in the presence of aluminium chloride,[3] by the action of carbon tetrachloride on benzene in the presence of aluminium chloride followed by hydrolysis.[4]

[1] Peligot, Ann. **12**, 41 (1834); Chancel, **72**, 279 (1849).

[2] Friedel and Crafts, Ann. chim. phys. (6), **1**, 510 (1884); Böeseken, Rec. trav. chim., **19**, 21 (1900); Olivier, **37**, 205 (1917); Norris, Thomas and Brown, Ber. **43**, 2959 (1910); Rubidge and Qua, J. Am. Chem. Soc. **36**, 735 (1914).

[3] Friedel and Crafts, Ann. chim. phys. (6) **1**, 518 (1884); Friedel, Crafts and Ador, Ber. **10**, 1854 (1877).

[4] Böeseken, Rec. trav. chim. **24**, 3 (1905); Gomberg and Jickling, J. Am. Chem. Soc. **37**, 2577 (1915).

## IX

## BENZOYLHYDROPEROXIDE

$$(C_6H_5CO)_2O_2 + C_2H_5ONa \rightarrow C_6H_5COO_2Na + C_6H_5CO_2C_2H_5$$

$$C_6H_5COO_2Na + H_2SO_4 \rightarrow C_6H_5COO_2H + NaHSO_4$$

Submitted by M. Tiffeneau.
Checked by Roger Adams and F. E. Kendall.

### 1. Procedure

In a 5-l. round-bottom flask, fitted with an efficient mechanical stirrer and surrounded by an ice-salt mixture, is placed a solution of 121 g. (0.5 mole) of pure dry finely-powdered benzoylperoxide (m.p. 104°) (Note 1) in about 1.5 l. of dry toluene. The temperature should be below −5°. A solution of sodium ethylate, prepared by dissolving 23 g. (1 mole) of sodium in 500 cc. of absolute alcohol, and cooled to 0°, is introduced from a separatory funnel while the mixture is vigorously stirred. This operation should not require more than eight or ten minutes. The liquid whitens and thickens considerably on account of the formation of sodium benzoylperoxide.

After the sodium ethylate has been added, the sodium benzoylperoxide is dissolved by pouring 2 l. of ice water into the flask, while continuing the stirring and keeping the mixture cold (Note 2). When there remains no more than a trace of sodium benzoylperoxide, as evidenced by the fact that addition of a small quantity of ice water produces no further clarification, the toluene layer is separated in a previously cooled separatory funnel. The aqueous solution is extracted with ether which takes up the ethyl benzoate, the ether is separated, and the

aqueous portion placed in the original flask surrounded by the cooling mixture. The liquid should be clear and absolutely free from unchanged benzoylperoxide.

The solution is cooled to 0° and then a cold solution of 54 g. of sulfuric acid (sp. gr. 1.84) in 50 cc. of water (slightly more than the theoretical amount) is slowly introduced from the separatory funnel during vigorous stirring. The solution becomes turbid and whitens as a result of the formation of the hydroperoxide, but no solid should appear. There should be no evolution of gas. Oxygen is evolved if the cooling is insufficient. The hydroperoxide appears in the form of a thick oil. The mixture is poured into a separatory funnel and extracted three times with 250-cc. portions of cold chloroform (Note 3) which dissolves the hydroperoxide. The chloroform is poured into a graduated cylinder, the volume noted, then poured into a carefully dried flask containing anhydrous sodium sulfate. The yield is 750–820 cc. of a solution containing 40 g. of benzoylhydroperoxide (90 per cent of the theoretical amount) (Notes 4 and 5). The use of this reagent in oxidation reactions is illustrated by the formation of styrene oxide from styrene (p. 84).

## 2. Notes

1. The benzoylperoxide used was analyzed by dissolving 1 g. in 25 cc. of dry ether and adding 2 cc. of 5 per cent sodium ethylate solution, keeping the temperature below −5°. The ether solution was extracted with exactly 100 cc. of cold water and an aliquot part of the aqueous extract taken. To this was added 2 cc. of 5 per cent potassium iodide and 2 cc. of dilute hydrochloric acid and the liberated iodine was titrated with 0.1 N sodium thiosulfate solution. The peroxide analyzed 90 per cent pure.

2. Generally it is noticed that a little of the benzoylperoxide remains undissolved, causing a turbidity in the bottom of the flask. This does not interfere with the reaction.

3. Ethereal solutions of the hydroperoxide are as stable as

chloroform solutions, but have been found to be notably less active.

4. Determination of active oxygen: The equation

$$C_6H_5COO_2H + 2\,KI + HCl \rightarrow C_6H_5CO_2K + I_2 + KCl + H_2O$$

shows that 16 g. of active oxygen correspond to 2 x 127 g. of iodine. Suppose for simplicity that a solution of sodium thiosulfate which is exactly 0.1 N is available. One cc. of this solution, containing 0.158 g. of sodium thiosulfate, corresponds to 0.0008 g. of active oxygen. Let $v$ be the total volume of the chloroform solution of benzoylhydroperoxide prepared. For titration, 0.5 cc. of this solution is taken and several drops of dilute hydrochloric acid added. If $n$ cc. of thiosulfate is required to absorb the iodine set free, the weight of active oxygen may be found from the following equation: $p = nv\,\frac{.0008}{0.5}$ or $p = \frac{nv}{625}$.

5. The yield is calculated upon the benzoylperoxide content of the material used. A decrease in the size of the run decreases the yield of benzoylhydroperoxide. A run using 20 g. of benzoylperoxide gave a yield of 65 per cent of the theoretical amount.

6. A recent publication by Hibbert and Burt [1] has modified Tiffeneau's directions, particularly in regard to the order of addition of the reacting substances. Tiffeneau adds the sulfuric acid to the sodium benzoylperoxide while Hibbert and Burt use the reverse procedure. The latter investigators state "benzoylhydroperoxide is very unstable in the presence of alkali, and its preparation must therefore be carried out in such a manner that no trace of sodium hydroxide is in solution when the free hydroperoxide is liberated. This is practically impossible when separation is effected by adding the acid to the aqueous solution of the sodium benzoylperoxide. When the latter is precipitated in ether solution by the action of sodium ethylate on the benzoylperoxide, the sodium salt always carries down with it a small amount of the ethylate and the latter during the acidification process yields sufficient free alkali to bring about a decomposition of the hydroperoxide as fast as it is formed. The reverse order is therefore employed."

Hibbert and Burt dissolved the benzoylperoxide in dry ether, cooled to $-5°$ and added the calculated amount of a 10 per cent sodium ethylate solution, maintaining the low temperature during the procedure. Sufficient ice water was added to give a clear solution, the ether containing the ethyl benzoate separated and the aqueous sodium benzoylperoxide solution added slowly with stirring to twice the necessary amount of cold 20 per cent sulfuric acid (reaction mixture always at 0°). The oily layer of benzoylhydroperoxide was then extracted three times with chloroform and the extract dried over anhydrous sodium sulfate.

This procedure was carried out by the checkers and compared with Tiffeneau's procedure. Tiffeneau's directions seem preferable for the following reasons. There was much less tendency to form an emulsion when the sodium salt was extracted with ether. The emulsion in Hibbert's methods was frequently persistent and the solution became warm before the aqueous solution could be separated from the ether, thus causing decomposition. A 10 per cent solution of sodium ethylate is difficult to handle for it crystallizes and cannot be added from a separatory funnel. If more alcohol is added the tendency toward formation of the emulsion is increased.

It seems to the checkers that if any free alkali were present with the sodium benzoylperoxide this would certainly be neutralized first when acid is added before any free benzoylhydroperoxide is formed. At any rate the yields by both procedures were excellent.

7. Evaporation of a chloroform solution of benzoylhydroperoxide under reduced pressure yields a paste containing 20–30 per cent of hydroperoxide. On further evaporation this decomposes into benzoic acid. A chloroform solution of benzoylhydroperoxide when carefully dried over anhydrous sodium sulfate at 0° may be kept exposed to light at room temperature for a number of days without appreciable decomposition. In order to obtain benzoylhydroperoxide free from the reagents used in its preparation, it is necessary to extract the product with chloroform, such extraction resulting in a loss of about 10 per cent.

## 3. Methods of Preparation

Benzoylhydroperoxide has always been prepared by the action of sodium ethylate on benzoylperoxide and subsequent acidification with dilute sulfuric acid.[2]

[1] Hibbert and Burt, J. Am. Chem. Soc. **47**, 2240 (1925).

[2] Baeyer and Villiger, Ber. **33**, 858, 1569 (1900).

# X

## BENZYLACETOPHENONE

$$C_6H_5CH{=}CHCOC_6H_5 + H_2(Pt) \rightarrow C_6H_5CH_2CH_2COC_6H_5$$

Submitted by ROGER ADAMS, J. W. KERN and R. L. SHRINER.
Checked by HENRY GILMAN and S. A. HARRIS.

### 1. Procedure

A SOLUTION of 20.8 g. (0.1 mole) of benzalacetophenone (Note 1) (Org. Syn. 2, 1) in 150 cc. of C.P. ethyl acetate (Note 2) is placed in the reaction bottle of the catalytic reduction apparatus (p. 10) and 0.2 g. of platinum oxide catalyst (p. 92) is added. The apparatus is evacuated, then filled with hydrogen, and the mixture shaken with hydrogen until 0.1 mole has been absorbed. The time required is usually about fifteen to twenty-five minutes (Note 3). The platinum is filtered off and the solvent removed from the filtrate by distillation. The benzylacetophenone is recrystallized from about 25 cc. of alcohol and melts at 72–73°. The yield is 17–20 g. (81–95 per cent of the theoretical amount).

### 2. Notes

1. The benzalacetophenone should be freshly recrystallized from alcohol just before using and should melt at 57°.

2. Owing to the comparatively slight solubility of benzalacetophenone in alcohol, ethyl acetate is used as a solvent during the reduction.

3. If 0.1 g. of catalyst is used the reduction requires about three hours; an increase in catalyst to 0.5 g. causes the reduction to take place in three or four minutes. The exact time depends

to a considerable extent on the grade of benzalacetophenone used and it is not certain that the very purest will necessarily be reduced in the shortest time.

### 3. Methods of Preparation

Benzylacetophenone has been prepared by the reduction of benzalacetophenone with zinc and acetic acid [1] and catalytically with palladium and hydrogen;[2] by the reduction of β-duplobenzylidene acetophenone monosulfide;[3] by the oxidation of the corresponding carbinol with chromic acid;[4] by the hydrolysis of ethyl benzyl benzoylacetate;[5] from acetophenone and benzyl chloride by the action of sodamide;[6] and from benzoic and hydrocinnamic acids using as catalysts manganese oxide [7] and ferric oxide.[8]

[1] Schneidewind, Ber. **21**, 1325 (1888); Harries and Hübner, Ann. **296**, 327 (1897).

[2] Straus and Grindel, Ann. **439**, 294 (1924).

[3] Fromm, Ber. **41**, 3648 (1908).

[4] Bauer, Compt. rend. **154**, 1094 (1912).

[5] Perkin and Stenhouse, J. Chem. Soc. **59**, 1007 (1891).

[6] Claisen, Ber. **38**, 698 (1905); Haller and Bauer, Compt. rend. **149**, 8 (1909).

[7] Sabatier and Mailhe, Compt. rend. **158**, 835 (1914).

[8] Mailhe, Bull. soc. chim. (4) **15**, 325 (1914).

## XI

## BENZYLANILINE

$$C_6H_5CH_2Cl + C_6H_5NH_2 \rightarrow C_6H_5CH_2NHC_6H_5 + HCl$$

Submitted by F. G. WILLSON and T. S. WHEELER.
Checked by HENRY GILMAN and R. MCCRACKEN.

### 1. Procedure

A 1500-cc. flask is fitted with a reflux condenser, a mechanical stirrer, and a 200-cc. separatory funnel. In the flask are placed 372 g. (4 moles) of aniline (Note 1), 105 g. (1.25 moles) of sodium bicarbonate (Note 2) and 100 cc. of water. The flask and contents are then heated on a steam bath to 90–95°, and 127 g. (1 mole) of benzyl chloride (Note 3) is run in slowly from the separatory funnel, vigorous agitation being maintained. The addition of benzyl chloride should take not less than one and one-half to two hours, and the reaction is complete in four hours.

The mixture is then cooled, filtered with suction, the layers of water and organic liquid separated, and the latter washed with saturated salt solution (Note 4). The amines are then dried by shaking with about 20 g. of anhydrous sodium sulphate, and again filtered with suction. The excess of aniline is removed by vacuum distillation (Note 5) using a modified Claisen flask with a fractionating side arm (Org. Syn. **1**, 40). The aniline distils at 81°/12 mm., and then the temperature rises quickly to the boiling point of benzylaniline, 180°/12 mm. or 190°/16 mm. When the temperature has risen to within about 5° of the boiling point of the benzylaniline, the receiver is again changed and the benzylaniline collected from 170–200°/12 mm., prac-

tically all boiling at 178–180°/12 mm. The aniline recovered amounts to 250–260 g. (89–92 per cent of the theoretical amount), and the yield of benzylaniline is 155–160 g. (85–87 per cent of the theoretical amount based on the benzyl chloride). The product solidifies on cooling and melts at 33–36°. It is practically colorless and sufficiently pure for most synthetic purposes. A pure compound melting at 36° may be obtained by crystallizing the product from about 100 cc. of ligroin (b.p. 85–90°). The solution is cooled in a freezing mixture to cause crystallization, the crystals filtered with suction, washed with a little cold ligroin, pressed, and dried. The recovery is about 90 per cent of the original product.

## 2. Notes

1. Benzylaniline reacts with benzyl chloride to form dibenzylaniline. If the proportion of aniline used is less than that given, the yield of benzylaniline is lowered, and separation rendered more difficult.

2. Sodium bicarbonate is used on account of its high purity and convenience in handling. An equivalent amount of the normal carbonate may be substituted, but reagents of stronger basicity increase the proportion of high-boiling by-products.

3. The benzyl chloride should be freshly distilled and collected at 176–178°.

4. Saturated salt solution is used here in preference to water, as separation of the liquids is more rapid and clean.

5. The aniline may also be quite satisfactorily removed by distillation under atmospheric pressure, using an efficient fractionating column, the distillation being interrupted when the thermometer in the still head registers 235°.

6. Benzylaniline distils without appreciable decomposition at atmospheric pressure at 298–300°. It assumes, however, a yellow color, and separation from any higher-boiling impurities is more difficult than when distillation is carried out under reduced pressure.

### 3. Methods of Preparation

Fleischer[1] prepared benzylaniline by heating aniline with benzyl chloride at 160°. This reaction may be very violent and always leads to mixtures. Bernthsen and Trompetter[2] reduced thiobenzanilide with zinc and hydrochloric acid or sodium amalgam, while O. Fischer[3] reduced benzalaniline with sodium and alcohol, to benzylaniline. Knoevenagel[4] obtained a 32 per cent yield of benzylaniline from benzyl alcohol and aniline in the presence of iodine. Ullmann[5] describes the preparation of benzylaniline from benzyl chloride and excess of aniline at low temperatures.

[1] Fleischer, Ann. **138**, 225 (1866).

[2] Bernthsen and Trompetter, Ber. **11**, 1760 (1878).

[3] Fischer, Ann. **241**, 330 (1887).

[4] Knoevenagel, J. prakt. Chem. (2) **89**, 32 (1914).

[5] Ullmann, "Enzyklopädie der technischen Chemie" (Urban and Schwarzenberg, Berlin) I, 445 (1914).

XII

# $p$-BROMODIPHENYL

$$p\text{-}BrC_6H_4N_2Cl + C_6H_6 + NaOH \rightarrow$$
$$p\text{-}BrC_6H_4C_6H_5 + N_2 + NaCl + H_2O$$

Submitted by M. GOMBERG and W. E. BACHMANN.
Checked by C. S. MARVEL and L. T. SANDBORN.

## 1. Procedure

FORTY-THREE grams (0.25 mole) of $p$-bromoaniline (Note 1) and 20 cc. of water are warmed in a 400-cc. beaker until the bromoaniline melts, and then 50 cc. of concentrated hydrochloric acid (sp. gr. 1.19) is added with mechanical stirring. The mixture is heated and stirred until solution is practically complete (Note 2). The beaker is then set in a dish of ice water and the solution is stirred as it cools in order to precipitate the $p$-bromoaniline hydrochloride in fine crystals. A few small pieces of ice are added and the cold (about 0–5°) suspension is diazotized with a solution of 18 g. of sodium nitrite in 36 cc. of water to an end point with starch-iodide paper.

The diazotized solution is poured into a 1.5-l. wide-mouth flask or bottle which is surrounded by ice water. Three hundred cc. of cold benzene is now poured into the diazonium solution, and by means of a good stirrer the two liquids are intimately mixed. The mixture, which is at the temperature of melting benzene, is now ready for the addition of alkali.

To this well-stirred mixture is added 58 cc. of 5 N sodium hydroxide solution over a period of one-half to three-quarters of an hour. This may be added drop by drop from a separatory funnel or in portions of a few cubic centimeters. The addition of the alkali causes the formation of a yellow precipitate which,

on being stirred into the benzene, reacts with the latter and gives *p*-bromodiphenyl. If too much of this reactive "oxide" is precipitated at one time, some of it may decompose to a dark-brown product. The alkali is, therefore, added at such a rate that the amount of precipitate is at no time greater than can readily react with the benzene, and the stirring must be efficient. The temperature during the reaction is kept at about 5°; when all the alkali has been added, the mixture is allowed to warm to room temperature.

If an emulsion has formed, it may be broken by acidifying with hydrochloric acid, whereupon two clear layers are obtained. The benzene solution may be dried and then fractionated or preferably, it may be steam distilled. In the latter case it is transferred to a 1-l. Claisen flask, the flask is set in an oil bath (Note 3) and the benzene distilled. Steam is then passed in, and after the last of the benzene is removed, the *p*-bromodiphenyl distils with the steam. The temperature of the oil bath is held at 170° in order to hasten the distillation. The product solidifies in the condenser and receiving flask. There is obtained 23–24 g. of *p*-bromodiphenyl which melts at 85–86.5°.

The crude product is usually yellow or orange in color. The color may be readily removed by dissolving the crude product in 200 cc. of hot ethyl alcohol and treating this solution with 5 g. of zinc dust and about 5 cc. of concentrated hydrochloric acid (sp. gr. 1.19). This solution is then filtered and the *p*-bromodiphenyl allowed to crystallize. This gives a white product melting at 89.5–90°. The yield is 20–21 g. (34–35 per cent of the theoretical amount).

## 2. Notes

1. The *p*-bromoaniline used was somewhat colored and melted at 62.5–63°.

2. The volume of the diazonium solution is kept as small as possible in order that the proportion of benzene to water may be as large as possible. The bromoaniline does not completely dissolve in this quantity but is entirely converted to the salt.

3. There is some tendency toward foaming during the steam distillation. To avoid this the flask should be submerged almost completely in the oil bath.

### 3. Methods of Preparation

*p*-Bromodiphenyl has been obtained along with some of the ortho derivative from the bromination of diphenyl.[1] However, according to Schlenk,[2] the product so obtained is contaminated with some *p, p'*-dibromodiphenyl which is very difficult to remove. Bamberger obtained *p*-bromodiphenyl from the action of benzene on solid *p*-bromobenzene diazoanhydride.[3] The method described in the procedure has recently been described in the literature.[4]

[1] Schultz, Ann. **174**, 207 (1874).
[2] Schlenk, Ber. **46**, 1477 (1913).
[3] Bamberger, Ber. **29**, 470 (1896).
[4] Gomberg and Bachmann, J. Am. Chem. Soc. **46**, 2339 (1924).

XIII

## *m*-BROMONITROBENZENE

$$C_6H_5NO_2 + Br_2(Fe) \rightarrow m\text{-}BrC_6H_4NO_2 + HBr$$

Submitted by John R. Johnson and C. G. Gauerke.
Checked by Frank C. Whitmore and T. Otterbacher.

### 1. Procedure

In a 3-l. three-neck, round-bottom flask, provided with an efficient reflux condenser bearing an outlet tube held above a surface of water, a 100-cc. separatory funnel, and a mercury-sealed mechanical stirrer (Note 1), is placed 270 g. (2.2 moles) of freshly distilled dry nitrobenzene (Note 2). The joints in the apparatus are made of asbestos paper covered with water glass (Org. Syn. 5, 9). The flask is heated in an oil bath maintained at 135–145°, and 26 g. of iron powder and 180 cc. (3.5 moles) of dry bromine (Note 3) are added in the following manner: Eight grams of iron powder ("ferrum reductum") (Note 4) is added through the side neck to the stirred nitrobenzene. From the separatory funnel 60 cc. of bromine is added at such a rate that the bromine vapors do not traverse the condenser. This addition requires about one hour, and the mixture is stirred and heated for another hour before the addition of a second portion of iron and bromine. Two portions, each of 8 g. of iron powder and 60 cc. of bromine, are added under the same conditions as the first addition, and the mixture is stirred and heated for one hour between the completion of one addition and the beginning of another. The evolution of hydrogen bromide slackens considerably toward the last of the heating, and there is practically no more bromine vapor condensed.

A final addition of 2 g. of iron powder is made, and the heating continued for one hour longer.

The reaction product, which is a dark reddish-brown liquid, is poured or siphoned (Note 5) into 1.5 l. of water to which 50 cc. of a saturated solution of sodium bisulfite has been added (Note 6). The mixture is distilled with steam (Org. Syn. 2, 80) and the first portion of the distillate is collected separately to remove a small amount of unchanged nitrobenzene. It is necessary to collect about 12 l. of distillate in order to obtain all of the *m*-bromonitrobenzene. The yellow crystalline solid is filtered with suction and pressed well on the funnel to remove water and traces of nitrobenzene. The yield of crude product varies from 270–340 g. (60–75 per cent of the theoretical amount). It melts at 51.5–52° and boils at 117–118°/9 mm. This product is satisfactory for most purposes. If a purer material is desired, the crude *m*-bromonitrobenzene may be distilled under reduced pressure. The recovery on purification is about 85 per cent. Brühl recorded the b.p. as 138°/18 mm. and the m.p. as 56° for pure *m*-bromonitrobenzene.[1]

## 2. Notes

1. With small amounts, up to 90 g. of nitrobenzene, mechanical stirring is not essential, and occasional shaking is sufficient.

2. The nitrobenzene is dried by distillation under atmospheric or reduced pressure, by rejecting the first 5 per cent of the distillate.

3. The bromine is dried by shaking with an equal volume of concentrated sulfuric acid and separating.

4. A number of other forms of iron were used, but none gave as good results as the "ferrum reductum."

5. If a series of successive runs is to be made, it is convenient to siphon the reaction product, and carry out a second preparation in the same apparatus without dismantling it.

6. The sodium bisulfite is added to remove any free bromine. A large excess should not be used as secondary reactions may occur during the steam distillation.

### 3. Methods of Preparation

*m*-Bromonitrobenzene has been obtained through ***m*-nitro**benzene diazonium salts [2] and by elimination of the amino group from 4-bromo-2-nitroaniline.[3] It has been prepared by the bromination of nitrobenzene in the presence of various catalysts.[4]

The procedure given is adapted from that described by Wheeler and McFarland.[5]

[1] Brühl, Z. physik. Chem. **22**, 379 (1897).

[2] Griess, Phil. Trans. Roy. Soc. London **154, III,** 711 (1864); **Jahresber. 1866,** 457; Fittig and Mager, Ber. **8**, 364 (1875).

[3] Wurster, Ber. **6**, 1543 (1873); Wurster and Grubenmann, Ber. **7**, 416 (1874).

[4] Scheufelen, Ann. **231**, 165 (1885).

[5] Wheeler and McFarland, Am. Chem. J. **19**, 366 (1897).

## XIV

# *tert*-BUTYL CHLORIDE

$$tert\text{-}C_4H_9OH + HCl \rightarrow tert\text{-}C_4H_9Cl + H_2O$$

Submitted by JAMES F. NORRIS and ALANSON W. OLMSTED.
Checked by HENRY GILMAN and L. L. HECK.

### 1. Procedure

IN a 500-cc. separatory funnel are placed 74 g. or 95 cc. (1 mole) of *tert*-butyl alcohol (Note 1) and 247 cc. (3 moles) of c.p. concentrated hydrochloric acid (sp. gr. 1.19). After shaking, the layers are allowed to separate (fifteen to twenty minutes) and the upper layer is drawn off and washed first with a 5 per cent sodium bicarbonate solution, then with water until neutral to moist litmus paper (Note 2). The chloride is treated with 10 g. of calcium chloride and shaken thoroughly, then transferred to a 125-cc. distilling flask. It is then distilled, using a long water condenser. The fraction boiling at 49.5–52° weighs 72–82 g. (78–88 per cent of the theoretical amount).

### 2. Notes

1. As it is difficult to prepare *tert*-butyl alcohol free from water, 84 g. of the constant boiling mixture of the alcohol and water can be used. This mixture boils at 80°, contains 88.24 per cent alcohol when the distillation is carried out at 760 mm., and can be readily obtained by distilling a sample of the dilute alcohol.

2. The chloride is very slowly hydrolyzed by cold water.

### 3. Methods of Preparation

*tert*-Butyl chloride has been prepared by passing hydrogen chloride into the alcohol kept cold in a freezing mixture,[1] and by distilling a mixture of the alcohol and a large excess of concentrated hydrochloric acid.[2] The method given is an improvement of the latter as it takes less time and largely avoids loss of the very volatile product by reducing the number of operations involved.

[1] Boedtker, Bull. soc. chim. (3) **31**, 965 (1904).
[2] Norris, Am. Chem. J. **38**, 642 (1907).

## XV

# γ-CHLOROBUTYRONITRILE

$$ClCH_2CH_2CH_2Br + KCN \rightarrow ClCH_2CH_2CH_2CN + KBr$$

Submitted by Charles F. H. Allen.
Checked by C. S. Marvel and C. G. Gauerke.

## 1. Procedure

In a 2-l. three-neck, round-bottom flask, fitted with a stirrer, a reflux condenser and a separatory funnel are placed 82 g. (1.2 moles) of potassium cyanide (95 per cent) (Note 1) and 100 cc. of water. The mixture is warmed and stirred until the cyanide is completely dissolved. To this solution is added 350 cc. of 95 per cent alcohol, followed by 158 g. (1 mole) of trimethylene chlorobromide (Note 2), and the mixture is heated under a reflux condenser (best on a water bath) with stirring for about one and one-half hours.

The solution is cooled and then diluted with 450 cc. of water. The oily layer of chloronitrile is collected in about 80 cc. of chloroform and separated from the water solution. The chloroform solution is washed with about 125–150 cc. of calcium chloride solution (prepared by adding one volume of water to an equal volume of a saturated solution of crystallized calcium chloride) and once with 125–150 cc. of water, and then dried over fused calcium chloride.

The dried solution is then fractionally distilled in a modified 100-cc. Claisen flask (Org. Syn. 1, 40). The chloroform is removed by distilling at ordinary pressure until the temperature reaches 120° (Note 3). The remainder may be fractionated under ordinary pressure but it is better to use reduced pressure.

After two or three distillations the yield of pure product boiling at 93–96°/26 mm. (Notes 4 and 5) is 42–49 g. (60–70 per cent of the theoretical amount based on the chlorobromide used, or 40–47 per cent based on the total amount of chlorobromide taken). (Notes 5 and 6.)

## 2. Notes

1. An equivalent amount (58 g., 1.2 moles) of sodium cyanide dissolved in 90 cc. of water may be used instead of the potassium salt without materially altering the yields.

2. The trimethylene chlorobromide used boiled at 142–147°. It may be prepared in 75–85 per cent yields from trimethylene chlorohydrin (p. 112) by the general method for the preparation of alkyl bromides described in Org. Syn. 1, 1.

3. The chloroform fraction has a very strong odor of isonitrile. Only a trace is noted in the redistilled product.

4. When the distillation is carried out under ordinary pressures (about 745 mm.) the product boils at 194–197°.

5. The lower boiling fraction is mainly unchanged trimethylene chlorobromide and amounts to 15–20 g. It may be refractionated or used directly in a subsequent run. The high boiling residue is mainly trimethylene cyanide. If the residues from several runs are combined and redistilled an average of 6–7 g. per run of product boiling at 160–165°/26 mm. is obtained.

6. Larger runs have been made and the yields are proportional; thus a five-mole run gives 210–245 g. of chlorobutyronitrile and 30–35 g. of trimethylene cyanide.

## 3. Methods of Preparation

γ-Chlorobutyronitrile has always been prepared by the action of potassium cyanide on trimethylene chlorobromide.[1]

[1] Henry, Compt. rend. **101**, 1158 (1885); Bull. soc. chim. (2) **45**, 341 (1886); Gabriel, Ber. **23**, 1771 (1890); **42**, 1252 (1909); Conant, Segur and Kirner, J. Am. Chem. Soc. **46**, 1884 (1924).

XVI

## β-CHLOROPROPIONIC ACID

$$CH_2=CHCHO+HCl \rightarrow CH_2ClCH_2CHO$$

$$CH_2ClCH_2CHO+O(HNO_3) \rightarrow CH_2ClCH_2CO_2H$$

Submitted by C. Moureu and R. Chaux.
Checked by C. S. Marvel and L. F. Martin.

### 1. Procedure

In a tared Erlenmeyer flask surrounded by an ice-salt bath is placed 100 g. (1.78 moles) of acrolein (Org. Syn. **6**, 1) (Note 1). When the temperature has dropped to $-10$ to $-15°$ a current of dry hydrogen chloride (Org. Syn. **6**, 64) is passed into the acrolein until it shows a gain in weight of 65 g. (1.78 moles). This requires about two hours. The product thus obtained is a clear, viscous, slightly yellow liquid which becomes very turbid and dark colored on standing one or two days (Note 2).

The oxidation of the crude β-chloropropionaldehyde is carried out in a 200-cc. flask fitted with a cork stopper held by a clamp about 2 cm. above the opening of the neck. The stopper carries a mechanical stirrer, a separatory funnel, a thermometer and a glass delivery tube about 10 mm. in diameter which is connected to a water pump. The space between the stopper and the flask is closed by winding a strip of asbestos paper around it (Note 3).

In the flask is placed 64 g. of fuming nitric acid (sp. gr. 1.49) (Note 4), the stirrer is started and about one-sixth (Note 5) of the crude β-chloropropionaldehyde is added (Note 6) very slowly through the separatory funnel. About 1 cc. of the aldehyde is added to the acid. The temperature remains constant for one or two minutes and then slowly rises. As the oxidation

begins, oxides of nitrogen are evolved and are drawn off by means of the water pump. When the temperature of the reaction mixture reaches about 30° (Note 7), the flask is immersed in a water bath (at about 15–20°) and the rate of addition of the aldehyde is regulated so that the temperature of the reaction mixture is about 30–35°. After the addition of the last of the portion of the aldehyde, stirring is continued until the temperature drops below 25°. This oxidation requires about twenty-five minutes.

The products of six successive oxidations are combined in a 1-l. long-neck flask. Oxides of nitrogen are often evolved but there is no danger of a violent reaction. The entire quantity of liquid is heated gradually on a water bath until the bath is boiling. This should be done under a hood as large quantities of oxides of nitrogen are evolved. After about an hour and a half the oxidation is complete and a yellow-brown liquid remains.

The liquid is placed in a modified Claisen flask (Org. Syn. 1, 40) and distilled (Note 8) on an oil bath with a water pump, care being taken to protect the manometer (placed in shunt in order to avoid the passage of a current of vapors) by a tube containing solid sodium hydroxide. A water condenser 40–50 cm. long should be used. At first oxides of nitrogen are evolved and it is difficult to obtain a low pressure. Then the pressure drops (to about 20–25 mm.) and nitric acid distils at 40–70°. When the distillation has nearly stopped, the temperature of the bath is raised until the boiling point of the distilling vapors reaches 100°. This fraction weighs 160–170 g. and is nitric acid having a sp. gr. of 1.25–1.30. It may contain a small amount of acrylic acid. The condenser is now removed from the apparatus, a distilling flask attached as receiver, and the residue is fractionated at 20 mm., collecting about 4–5 g. boiling up to 105° and 116–125 g. of β-chloropropionic acid boiling at 105–107° (60–65 per cent of the theoretical amount). The product melts at 35–40° (purest acid melts at 42°). The fraction boiling below 105° contains a large proportion of β-chloropropionic acid and should be redistilled with a subsequent run.

## 2. Notes

1. The acrolein used by the checker was that obtained by distilling the commercial material (stabilized by hydroquinone) purchased from Poulenc Frères.

2. β-Chloropropionaldehyde is a very unstable substance which polymerizes rapidly especially in the presence of traces of hydrochloric acid. The crude material must be oxidized without delay as standing before oxidation will cause a lowering of the yield.

3. This constitutes a safety device, since it prevents diffusion of the oxides of nitrogen, but in case the reaction becomes violent it permits a free expansion of a sudden wave of gases.

4. The concentration and purity of the fuming nitric acid is of considerable importance. It should have a sp. gr. of not less than 1.49 and should leave no residue on distillation.

5. It is not advantageous to work with larger quantities as an explosive reaction is liable to occur if stirring is stopped.

6. It is absolutely necessary to introduce the aldehyde into the nitric acid. When the reverse is attempted the reaction starts slowly but soon becomes explosive.

7. The temperature interval most favorable for the reaction is 30–35°.

8. The reaction mixture may also be worked up by pouring it into water and extracting the β-chloropropionic acid with ether. This is less satisfactory as the nitric acid is lost and some of the β-chloropropionic acid remains in the water.

## 3. Methods of Preparation

β-Chloropropionic acid has been prepared by the hydrolysis of ethylene cyanohydrin with hydrochloric acid,[1] and by the oxidation of β-chloropropionaldehyde [2] or of trimethylene chlorohydrin [3] by nitric acid.

[1] Jacobs and Heidelberger, J. Am. Chem. Soc. **39**, 1466 (1917).

[2] Krestownikow, Ber. **12**, 1487 (1879); Moureu, Bull. soc. chim. (3) **9**, 388 (1893); Ann. chim. phys. (7) **2**, 157 (1894); Moureu and Chaux, Bull. soc. chim. (4) **35**, 1360 (1924).

[3] Rojahn, Ber. **54B**, 3116 (1921); Adams and Marvel, Organic Chemical Reagents, Univ. of Ill. Bulletin, vol. 20, no. 8, p. 14 (1922); Powell, J. Am. Chem. Soc. **46**, 2879 (1924).

XVII

## β-CHLOROPROPIONIC ACID

$$ClCH_2CH_2CH_2OH + 2O(HNO_3) \rightarrow ClCH_2CH_2CO_2H + H_2O$$

Submitted by SARGENT G. POWELL.
Checked by C. S. MARVEL and STANLEY G. FORD.

### 1. Procedure

In a 1-l. wide-mouth, narrow bottle immersed in running water and fitted with a 3-hole rubber stopper holding a mechanical stirrer, a separatory funnel and a reflux condenser is placed 220 g. of concentrated nitric acid (sp. gr. 1.42). The condenser should be connected with a hood or trap to catch the oxides of nitrogen liberated during the oxidation. The stirrer is started and 50 g. (0.52 moles) of trimethylene chlorohydrin (p. 112) is added from the separatory funnel during the course of one hour. Stirring is continued for half an hour longer. During this part of the oxidation the reaction vessel is cooled with running water. The reaction is completed by warming the reaction mixture on a steam-bath for one hour.

The β-chloropropionic acid is best isolated by direct distillation under reduced pressure (Note 1) using a 250-cc. modified Claisen flask (Org. Syn. 1, 40). The nitric acid is collected up to 100°/20 mm. using a water condenser. The condenser is then removed and the residual β-chloropropionic acid is fractionated, collecting as pure product the portion boiling at 105–107°/20 mm. The yield is 31–31.5 g. (54–55 per cent of the theoretical amount) (Note 2). The product solidifies on cooling and melts at 41–41.5°.

## 2. Notes

1. About 130 cc. of nitric acid (sp. gr. 1.27) is obtained. If desired the oxidation mixture may be diluted with water and the β-chloropropionic acid extracted with ether and distilled. Some material is lost in the water by this procedure.

2. Larger runs may be carried out without lowering the yield. When a run of four times that described was made, the time of adding the trimethylene chlorohydrin was only doubled.

## 3. Methods of Preparation

These are given on p. 56.

## XVIII

## DIBENZOYLMETHANE

### (Phenyl-$\alpha$-hydroxystyrylketone)

$$C_6H_5CHBrCHBrCOC_6H_5 + 2NaOCH_3 \rightarrow C_6H_5C(OCH_3){=}CHCOC_6H_5 + 2NaBr + CH_3OH$$

$$C_6H_5C(OCH_3){=}CHCOC_6H_5 + H_2O \rightarrow C_6H_5C(OH){=}CHCOC_6H_5 + CH_3OH$$

$$C_6H_5C(OH){=}CHCOC_6H_5 \rightleftarrows C_6H_5COCH_2COC_6H_5$$

Submitted by CHARLES F. H. ALLEN.
Checked by ROGER ADAMS and G. R. YOHE.

### 1. Procedure

IN a 2-l. round-bottom flask, fitted with a stirrer and a reflux condenser, and surrounded by a cold water bath, are placed 184 g. (0.5 mole) of benzalacetophenone dibromide (Note 1) and 165 cc. of absolute methyl alcohol (Notes 2 and 3). A solution of sodium methylate, previously prepared by dissolving 23.2 g. of sodium (1.01 moles) in 230 cc. of absolute methyl alcohol, is added slowly through the condenser, stirring being begun as soon as the mass is fluid enough. When the addition has been completed, the whole is heated to boiling and refluxed for three hours. To the brown liquid is then added 140 cc. of water to dissolve the precipitated sodium bromide, and enough concentrated hydrochloric acid (sp. gr. 1.19) to acidify the solution, when the color changes to a light yellow and an oil separates. The acid solution is refluxed two hours longer, then cooled in ice-water, stirring rapidly to cause formation of small crystals (Note 5); the latter are separated by filtration

and washed once with 50 cc. of cold 50 per cent alcohol and then with water until free from acid. The yield (Note 1) of the crude, air-dried dibenzoylmethane, m.p. 76–78°, is 66–69 g. (59–61 per cent of the theoretical amount) (Note 4). The crude product is quite pure but if desired it may be recrystallized from 160 cc. of hot 95 per cent alcohol. The first crop weighs 58–62 g. (m.p. 77–78°) and on partial evaporation of the solvent a less pure second crop of 2–3 g. (m.p. 74–75°) can be obtained.

## 2. Notes

1. The yield depends largely upon the quality of the dibromide. The product which gave the results described in the procedure was prepared by dissolving 208 g. (1 mole) of benzalacetophenone (Org. Syn. **2**, 1) in 600 cc. of carbon tetrachloride, cooling the solution in an ice bath and adding with stirring 160 g. (1 mole) of bromine. After the reaction was complete the dibromide was filtered off and washed with two 250-cc. portions of hot alcohol. The product obtained in this way melted at 156–157° and weighed about 310 g.

2. If ordinary methyl alcohol is used, the yields agree with the lower figures. The diketone is also contaminated by an oily substance that persists through several recrystallizations. The presence of water favors the elimination of bromine and regeneration of the unsaturated ketone.

3. The use of ethyl alcohol results in an inferior product, m.p. 63–65°.

4. The use of steel spatulas should be avoided, as traces of iron salts cause the product to be of a reddish color. This can be removed either by a vacuum distillation, or by dissolving in concentrated sulfuric acid and reprecipitating by pouring the acid solution upon cracked ice.

5. The mother liquor contains only 2–3 g. more of the diketone, which can be separated as the copper derivative by shaking an ethereal extract with a saturated aqueous solution of copper acetate.

### 3. Methods of Preparation

Dibenzoylmethane has been prepared by the hydrolysis of dibenzoyl acetic acid;[1] by the slow spontaneous decomposition of acetyl dibenzoyl methane;[2] by the action of metallic sodium,[3] sodium ethylate,[3] sodium methylate,[4] alchoholic potash,[4] or sodamide[5] on mixtures of acetophenone and ethyl benzoate; and by the action of alcoholic potash,[6] sodium methylate,[7] or sodium ethylate[8] on benzalacetophenone dibromide.

[1] Baeyer and Perkin, Ber. **16**, 2134 (1883); Perkin, J. Chem. Soc. **47**, 250 (1885).
[2] Claisen, Ann. **291**, 83 (1896).
[3] Claisen, Ann. **291**, 52 (1896).
[4] Bülow and von Sicherer, Ber. **34**, 2372 (1901).
[5] Claisen, Ber. **38**, 696 (1905).
[6] Wislicenus, Ann. **308**, 219 (1899); See Abell, J. Chem. Soc. **101**, 1002 (1912).
[7] Pond, Maxwell and Norman, J. Am. Chem. Soc. **21**, 964 (1899).
[8] Sluiter, Rec. trav. chim. **24**, II, 368 (1905).

XIX

## DI-*o*-NITROPHENYL DISULFIDE

$$2\ o\text{-}ClC_6H_4NO_2 + Na_2S_2 \rightarrow o\text{-}NO_2C_6H_4SSC_6H_4NO_2 + 2NaCl$$

Submitted by MARSTON T. BOGERT and ARTHUR STULL.
Checked by FRANK C. WHITMORE, W. F. SINGLETON and F. E. SMITH.

### 1. Procedure

IN a 3-l. round-bottom flask fitted with a reflux condenser are placed 360 g. (1.5 moles) of crystalline sodium sulfide (Note 1) and 1.5 l. of 95 per cent alcohol. The flask is heated on a steam bath until the sulfide dissolves. Then 48 g. (1.5 moles) of finely ground sulfur is added, and the heating is continued until the sulfur has dissolved, forming a brownish red-solution of sodium disulfide (Note 2). A solution of 315 g. (2 moles) of *o*-chloronitrobenzene (Note 3) in 500 cc. of 95 per cent alcohol is prepared in a 5-l. round-bottom flask fitted with a reflux condenser. The sodium disulfide solution is added slowly to this solution through a funnel placed in the top of the reflux condenser. The addition should be slow until the violence of the reaction abates somewhat. The mixture is then heated on a steam bath, gently at first (Note 4), and then at full heat for two hours. After cooling, it is filtered by suction. The mixture of the organic disulfide and the sodium chloride is transferred to a 1-l. beaker and stirred thoroughly with 500 cc. of water to remove the sodium chloride. It is then filtered by suction and the crystalline residue is washed on the filter with 100 cc. of alcohol to remove any *o*-chloronitrobenzene. The product melting at 192–195° weighs 180–210 g. (58–66 per cent of the theoretical amount).

## 2. Notes

1. Crystals as dry as possible should be selected. If desired, an equivalent amount of analyzed fused sodium sulfide may be used. In this case, solution takes a longer time. Since an excess of sodium sulfide is added, slight inaccuracies in the amount used are not important.

2. In case a small amount of sodium disulfide separates in a layer at the bottom, it should be taken up with a little more alcohol and added to the chloronitrobenzene solution.

3. Commercial *o*-chloronitrobenzene containing 95–98 per cent of the ortho compound was used.

4. If too much heat is applied at first, the reaction becomes very violent.

## 3. Methods of Preparation

Di-*o*-nitrophenyl disulfide was first prepared by the action of hydriodic acid on *o*-nitrobenzene sulfochloride.[1] It has also been prepared by the reduction of *o*-nitrobenzene sulfinic acid with hydrogen bromide;[2] by the reduction of ethyl-*o*-nitrophenylsulfonacetate with ammonium sulfide;[3] and by the deamination of 4,4′-diamino-2,2′-dinitrodiphenyldisulfide.[4] The procedure given is the method of Blanksma[5] as elaborated by Wohlfahrt.[6]

[1] Cleve, Ber. **20**, 1534 (1887).

[2] Fries and Schürmann, Ber. **47**, 1199 (1914).

[3] Claasz, Ber. **45**, 1021 (1912).

[4] Müller, Z. f. Farbenind. **5**, 357 [Chem. Zentr. **1906**, II, 1587].

[5] Blanksma, Rec. trav. chim. **20**, 127 (1901).

[6] Wohlfahrt, J. prakt. Chem. (2) **66**, 553 (1902).

## ETHYL *p*-AMINOBENZOATE

$$p\text{-}NO_2C_6H_4CO_2C_2H_5 + 3H_2(Pt) \rightarrow p\text{-}NH_2C_6H_4CO_2C_2H_5 + 2H_2O$$

Submitted by ROGER ADAMS and F. L. COHEN.
Checked by HENRY GILMAN and S. A. HARRIS.

### 1. Procedure

A SOLUTION of 19.5 g. (0.1 mole) of ethyl *p*-nitrobenzoate (Note 1) in 150 cc. of 95 per cent alcohol is placed in the reaction bottle of the catalytic reduction apparatus (p. 10) and 0.2 g. of platinum oxide catalyst (p. 92) is added. The mixture is shaken with hydrogen until three molecular equivalents have been absorbed. The time required is about seven minutes. The platinum is filtered off and the alcohol removed from the filtrate by distillation. The ethyl *p*-aminobenzoate, recrystallized from about 40 cc. of ether, melts at 89–90°. The yield is 15–16.5 g. (91–100 per cent of the theoretical amount).

### 2. Notes

1. The ethyl *p*-nitrobenzoate should be freed from acid and recrystallized from alcohol until it melts at 57°.

### 3. Methods of Preparation

Ethyl *p*-aminobenzoate has been prepared by the esterification of *p*-aminobenzoic acid [1] and by the reduction of ethyl *p*-nitrobenzoate with ammonium sulfide.[2] Although commercially the reagent used is usually iron and water in presence of a little acid, in the laboratory the catalytic reduction as described in the procedure is by far the most convenient.

[1] Salkowski, Ber. **28**, 1921 (1895); Vorländer and Meyer, Ann. **320**, 135 (1902).
[2] Limpricht, Ann. **303**, 278 (1898).

XXI

## ETHYL BENZOYLFORMATE

$$C_6H_5CHOHCO_2H + O(KMnO_4) \rightarrow C_6H_5COCO_2H + H_2O$$

$$C_6H_5COCO_2H + C_2H_5OH(H_2SO_4) \rightarrow C_6H_5COCO_2C_2H_5 + H_2O$$

$$C_6H_5COCO_2C_2H_5 + NaHSO_3 \rightarrow C_6H_5COH(SO_3Na)CO_2C_2H_5$$

$$C_6H_5COH(SO_3Na)CO_2C_2H_5 + H_2SO_4 \rightarrow C_6H_5COCO_2C_2H_5 + NaHSO_4 + SO_2 + H_2O$$

Submitted by B. B. Corson, Ruth A. Dodge, S. A. Harris, and R. K. Hazen.
Checked by C. S. Marvel and F. E. Kendall.

### 1. Procedure

In a 12-l. earthenware crock equipped with an efficient stirrer and a strong motor are placed 375 g. (2.5 moles) of mandelic acid (Org. Syn. **6**, 58) and 500 cc. of water. The stirrer is started, and a cool solution of 110 g. (2.8 moles) of sodium hydroxide (or 115 g. of technical sodium hydroxide) in 500 cc. of water is added. This is followed by the addition of 2000 g. of cracked ice and then after a few minutes by 275 g. (1.74 moles) of finely ground U.S.P. potassium permanganate in portions over a period of half an hour. The mixture is stirred for one and a half hours, the temperature being maintained at $-2$ to $-4°$. About 5 kg. of ice is necessary. At the end of one and a half hours the mixture is tested for excess permanganate by placing a drop on a piece of filter paper; there is formed a black or brown center of manganese dioxide, a greenish ring around this, and an outer ring which is colorless in the absence and pink in the

presence of excess permanganate. Any excess is removed by adding ethyl alcohol, generally about 200–300 cc.

When the permanganate has been destroyed, the stirrer is stopped and the manganese dioxide allowed to coagulate for an hour. The mixture is filtered through two 20-cm. Büchner funnels, the filter cakes washed with 1000 cc. of water (Note 1) and sucked dry again (Note 2). The filtrate is evaporated to 800–1000 cc. over a free flame. While the volume of solution is large, two 30-cm. evaporating dishes are used, but toward the end the two solutions are combined in one dish. The evaporation requires two to three hours. Sometimes a little manganese dioxide will be coagulated during the evaporation and this should be removed by filtration.

The yellowish solution is transferred to a 3-l. round-bottom wide-neck flask and cooled with running water while 300 cc. of concentrated sulfuric acid is added slowly from a separatory funnel. This acidification process requires thirty minutes and the temperature should not rise much above 25°. The liquid froths and about 30 g. of benzoic acid separates but it is not filtered. Extraction of the reaction mixture with 200 cc. portions of ether until 1500 cc. of extract has been collected is now carried out in a separatory funnel. The ether is distilled on a steam bath from a 1-l. round-bottom wide-neck flask connected with a water condenser, the extract being added from a separatory funnel as fast as the ether distils. After most of of the ether has been removed, the heating is continued for an additional half hour.

The crude liquid acid (about 300 g.) is cooled with running water and 15 cc. of concentrated sulfuric acid is added; the clear yellow oil becomes cloudy. The acid is esterified by the method described in Org. Syn. 3, 54, with the following changes: all three flasks, the alcohol flask, the trap, and the esterification flask are 1-l. round-bottom wide-neck flasks. The alcohol flask and the trap are set on adjacent steam baths. The esterification flask is placed in an oil bath which is heated by a free flame. A safety tube leads from the alcohol flask and dips under 7.5 cm. of mercury contained in a side-arm tube.

This mercury safety valve avoids all dangers which might result from the development of excess pressure within the system (Note 3). The temperature of the esterification mixture is kept at 105–110° and ethyl alcohol vapor is passed through until 500 cc. of distillate has been collected. This requires about three hours. The distillate consists of alcohol, water, and a little ether.

The crude ester is cooled, an equal volume of benzene is added, then the free acid is neutralized by shaking with about 250 cc. of a 10 per cent solution of sodium carbonate (Note 4). The benzene solution is poured into 1300 cc. of a saturated solution of sodium bisulfite (about 60 g. of technical sodium bisulfite per 100 cc.), contained in a wide-neck bottle equipped with an efficient stirrer, and the mixture stirred for two and a half hours. The mixture soon warms up a little and becomes semi-solid. It is filtered through a 20-cm. Büchner funnel and carefully washed, first with 200 cc. of a saturated solution of sodium bisulfite, finally with two 150-cc. portions of benzene (Notes 5 and 6). The white pearly flakes of the sodium bisulfite addition product are transferred to a 3-l. round-bottom wide-neck flask equipped with a mechanical stirrer and containing 700 cc. of water, 175 cc. of concentrated sulfuric acid, and 500 cc. of benzene. The flask is heated on a steam bath under a hood, the temperature being kept at 55°, and the mixture is stirred for thirty minutes (Note 7). The solution is then poured into a separatory funnel, the benzene separated and the water layer extracted with a 200-cc. portion of benzene. The combined benzene solution is shaken with excess of 10 per cent sodium carbonate solution to remove free acid and sulfur dioxide (Note 8). The benzene is washed with a little water and then dried over anhydrous potassium carbonate (Note 9). The benzene is distilled at ordinary pressure over a free flame from a 500-cc. Claisen flask, the solution being added from a separatory funnel as fast as the benzene distils. It is advisable to distil the ester under reduced pressure although it can be done under ordinary pressure. The fraction distilling around 118°/5 mm., 130°/10 mm., 138°/15 mm., 148°/25 mm., 155°/35 mm., or

254°/760 mm., is collected. The yield of ethyl benzoylformate is 155–175 g. (35–40 per cent of the theoretical amount). (Note 10).

## 2. Notes

1. In order to wash the manganese dioxide cake it must be removed from the funnel and stirred into a thin paste with water.

2. It is advisable not to stop the experiment until after filtration since manganese dioxide slowly oxidizes benzoylformic acid to benzoic acid.

3. If it is necessary to generate the steam from a can or similar contrivance, the steam generator should be connected with a safety tube dipping under 20–25 cm. of mercury.

4. The sodium carbonate solution contains 8–15 g. of unesterified acid which can be easily recovered by acidification with concentrated hydrochloric acid followed by extraction with ether.

5. The benzene contains 80 g. of impure ethyl benzoate boiling at 180–260° and containing about 20 per cent of ethyl benzoylformate. In the case of the methyl ester the benzene contains 60 g. of impure methyl benzoate, boiling at 170–250°, and containing about 20 per cent of methyl benzoylformate.

6. If the stirring is not very efficient the benzene layer should be stirred with the bisulfite solution a second time.

7. Longer contact with acid tends to hydrolyze the ester. The reaction should be performed under a hood since considerable sulfur dioxide is generated.

8. This sodium carbonate solution contains about 4 g. of impure benzoylformic acid.

9. The potassium carbonate holds some ester which may be recovered by adding water and separating the ester layer.

10. The methyl ester is easily made by substituting methyl for ethyl alcohol. It boils at 250–255°/760 mm. The yield is about 175 g. (43 per cent of the theoretical amount).

11. This work was done with the aid of a grant from the

Cyrus M. Warren fund of the American Academy of Arts and Sciences.

## 3. Methods of Preparation

Ethyl benzoylformate has been prepared by the direct esterification of the acid[1] and by the action of oxides of nitrogen on an alcoholic suspension of indigo.[2] The acid has been prepared by many different reactions but the most practical are the hydrolysis of benzoyl cyanide,[3] the oxidation of acetophenone[4] and the oxidation of mandelic acid.[5]

[1] Claisen, Ber. **10**, 846 (1877); **12**, 629 (1879); Simon, Ann. chim. phys. (7) **9**, 529 (1896); Kailan, Monatsh. **28**, 1204 (1907); Acree, Am. Chem. J. **50**, 392, 393 (1913).

[2] Posner and Aschermann, Ber. **53*B***, 1931 (1920).

[3] Claisen, Ber. **10**, 429, 844 (1877); **12**, 626 (1879); Buchka, Ber. **20**, 395 (1887); Simon, Ann. chim. phys. (7) **9**, 508 (1896).

[4] Glücksmann, Monatsh. **11**, 248 (1890); Claus and Neukranz, J. prakt. Chem. (2) **44**, 80 (1891).

[5] Hunaeus and Zincke, Ber. **10**, 1489 (1877); Acree, Am. Chem. J. **50**, 391 (1913).

XXII

## ETHYL CYANOACETATE

$$ClCH_2CO_2Na + NaCN \rightarrow CNCH_2CO_2Na + NaCl$$
$$CNCH_2CO_2H + C_2H_5OH \rightarrow CNCH_2CO_2C_2H_5 + H_2O$$

Submitted by J. K. H. INGLIS.
Checked by C. S. MARVEL, W. F. TULEY and S. V. PUNTAMBEKER.

### 1. Procedure

IN a 5-l. round-bottom flask 500 g. (5.3 moles) of chloroacetic acid is dissolved in 700 cc. of water. The solution is warmed to 50° and neutralized with anhydrous sodium carbonate of which about 290 g. (2.6 moles) is required (a slight excess of sodium carbonate is not disadvantageous). Meanwhile 294 g. (5.8 moles) of sodium cyanide (97 per cent) is dissolved in 750 cc. of water warmed to 55°. The sodium cyanide solution is then added to the sodium chloroacetate solution, which has been cooled to room temperature, with rapid mixing of the two solutions and cooling under the water tap. The temperature rapidly rises; when it reaches 95° the solution should be cooled by adding 200 cc. of cold water and this repeated, if necessary, until the temperature no longer rises (Note 1). The solution is heated to the boiling point and boiled for five minutes (Note 2), and finally cooled with running water for a half hour.

The solution is filtered if not clear, and the cyanoacetic acid is set free (hood) by adding with thorough stirring 600 cc. (a slight excess) of commercial hydrochloric acid (sp. gr. 1.156). The solution is evaporated on a water bath at 60–70° (Note 3) under a pressure of 20–30 mm. and the evaporation continued until practically no more distillate (Note 4) comes over. To

the residue is added 600 cc. of 95 per cent alcohol. The solution is filtered (Note 5) from the sodium chloride, and the residue is washed with another 500-cc. portion of alcohol.

On evaporating the alcoholic solution under reduced pressure from a water bath held at 50–60° (Note 6) the residue weighs about 540 g. A mixture of 600 cc. of absolute alcohol and 10 cc. of concentrated sulfuric acid (Note 7) is then added. The mixture is then heated on the water bath under a reflux condenser for three hours. The excess of alcohol and some of the water formed are removed by distillation under reduced pressure and the residue again heated for two hours with 300 cc. of absolute alcohol and an additional 4 cc. of concentrated sulfuric acid. The alcohol is removed by distillation under reduced pressure, and when the ester has cooled to room temperature, the sulfuric acid is neutralized with a concentrated solution of sodium carbonate; the ester (upper layer) is separated, and the aqueous solution extracted with ether, or preferably benzene; about one-tenth of the yield is in the extract. The combined products are placed in a 1-l. distilling flask and distilled under reduced pressure after the solvent and alcohol and water have been removed. The ester is collected at 94–99°, chiefly at 97–98°/16 mm. (Note 8). The yield of a product analyzing about 97–98 per cent ethyl cyanoacetate amounts to 474–492 g. (77–80 per cent of the theoretical amount) (Note 9).

## 2. Notes

1. If the reaction between the cyanide and chloroacetate becomes too vigorous, hydrogen cyanide is set free and partly changed to brown material and a corresponding amount of glycollate is formed.

2. The color at this stage should be yellow or a light brown.

3. If the mixture is heated to a higher temperature there is a considerable loss due to decomposition of the cyanoacetic acid.

4. Toward the end of the distillation, hydrochloric acid should be present in the distillate if excess was added in the first place. During the addition of the hydrochloric acid the excess of cyanide is decomposed, giving off hydrogen cyanide.

5. It is much easier to remove the salt by means of a centrifuge. If this method is used the salt should be washed first with 500 cc. and then with 250 cc. of alcohol.

6. The solution containing mineral acid must not be evaporated at a high temperature or ethyl malonate will be formed.

7. The addition of sulfuric acid will probably produce a slight precipitate, but this may be ignored if the original treatment with hydrochloric acid was properly carried out.

8. Ethyl cyanoacetate boils at 97°/16 mm., 101°/19 mm., 107°/27 mm.

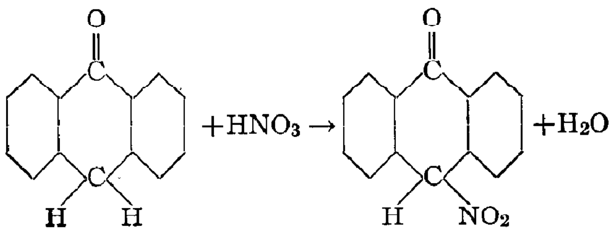
9. The product was analyzed for nitrogen by the Kjeldahl method.

### 3. Methods of Preparation

The method described differs from that given in Org. Syn. 3, 53 mainly in the use of hydrochloric acid in place of sulfuric acid, in the liberation of the cyanoacetic acid from the sodium salt and in the simplified esterification process. These are slight but very important differences and make the procedure much easier to carry out in the laboratory. Moreover, the yields are higher.

XXIII

## NITROANTHRONE



Submitted by Kurt H. Meyer.
Checked by J. B. Conant and W. C. Boyd.

### 1. Procedure

In a 1-l. beaker equipped with a separatory funnel, a mechanical stirrer, and a thermometer, 20 g. (0.1 mole) of anthrone (p. 8) is dissolved in 300 cc. of glacial acetic acid. While the mixture is kept at 60° and stirred, a solution of 7 cc. of fuming nitric acid (sp. gr. 1.5) in 50 cc. of glacial acetic acid is run in during one hour.

On cooling (to about 10°) 15 g. of nitroanthrone separates out in long yellowish-white needles. After the addition of 100 cc. of water to the mother liquor 6 g. more, somewhat darker in color, crystallizes in three to four hours.

On recrystallization from about 300 cc. of a 1 : 1 benzene-petroleum ether (40–60°) mixture, 16.5 g. of nitroanthrone melting at 140° (corr.) is obtained (67 per cent of the theoretical amount) (Note 1).

### 2. Notes

1. By dissolving in hot alkali (about 300 cc. of water and 30 g. of sodium hydroxide per gram of nitroanthrone) and precipitat-

ing with acid below 10°, the red nitroanthranol may be obtained, which on standing slowly changes back to the nitroanthrone.

### 3. Methods of Preparation

Nitroanthrone has been prepared by the nitration of anthracene in isobutyl alcohol,[1] and by the nitration of anthrone.[2]

[1] Perkin and Mackenzie, J. Chem. Soc. **61**, 868 (1892); Meisenheimer and Connerade, Ann. **330**, 177 (1904).

[2] Meyer and Sander, Ann. **396**, 149 (1913).

XXV

## PHENYLETHYLENE

### (Styrene)

$$C_6H_5CH=CHCO_2H \rightarrow C_6H_5CH=CH_2+CO_2$$

Submitted by T. W. ABBOTT and JOHN R. JOHNSON.
Checked by H. T. CLARKE and M. R. BRETHEN.

### 1. Procedure

IN a 500-cc. flask fitted with a 24-cm. fractionating column (Notes 1 and 4) attached to a water-jacketed condenser, are placed 148 g. (1 mole) of dry powdered cinnamic acid, 2 g. of hydroquinone and several small pieces of clay plate. One half gram of hydroquinone is also placed in the flask in which the distillate is to be collected (Note 2). The acid is rapidly heated over a wire gauze with a free flame until phenylethylene begins to distil, the heating being regulated so that the temperature of the vapors at the head of the column never exceeds 130°, and mainly remains below 120° (Notes 3 and 4). The cinnamic acid refluxes, but very little should escape and collect in the condenser. The decomposition is complete in three and one-half to five hours, when no more phenylethylene distils and the temperature at the head of the column rises rapidly. The distillate consists of a straw-colored oil and a little water; a dark tarry residue (50–60 g.) remains in the reaction flask. About 100 cc. of water is added to the distillate and the aqueous mixture is distilled. The phenylethylene is easily volatile with steam and separates in the distillate as a colorless oil. The oil (45–48 g.) is separated, dried with a small amount of calcium chloride, and carefully distilled under diminished pressure, cool-

ing the condenser and receiver to 0–5° by means of iced (or very cold) water. The phenylethylene is collected at 44–46°/40 mm. or 60–63°/60 mm. (Note 5). The yield is 40–42 g. (38–41 per cent of the theoretical amount) (Note 6).

## 2. Notes

1. The column consists of a glass tube of 13–14 mm. internal diameter, 24 cm. long from lower end to the side arm, which has an internal diameter of 7 mm. It is important that these dimensions be observed in order to avoid polymerization of the product. It has been found in checking that better results are obtained by making indentations in the tube at frequent intervals and at different angles; these tend to reduce the number of cinnamic acid particles which are carried over with the vapor. A column of the Vigreux type would no doubt also be suitable.

2. An anti-oxygen such as catechol or hydroquinone is used to prevent polymerization. Hydroquinone should be added in the ratio of one part per thousand unless the phenylethylene is to be used immediately.[1]

3. If the temperature of the escaping vapor rises above 130° appreciable amounts of cinnamic acid pass into the condenser and the yield falls materially.

4. If the fractionating column does not have the exact dimensions designated in Note 1 the temperature of the vapors at the head of the column will vary from those given. However, no difficulty will arise in obtaining the yield of product indicated if the general directions for heating the cinnamic acid, so as to avoid the carrying of the cinnamic acid into the distillate, are followed.

5. Phenylethylene should not be distilled under atmospheric pressure since the temperature (146°) required for the distillation causes a considerable loss by polymerization. The decomposition of cinnamic acid cannot be effected by distillation under diminished pressure, since the acid under these conditions distils below the temperature required for decomposition (approximately 300°).

# XXIV

## *m*-NITROPHENOL

$$m\text{-}NO_2C_6H_4NH_2 + H_2SO_4 + HNO_2 \rightarrow NO_2C_6H_4N_2OSO_3H$$

$$NO_2C_6H_4N_2OSO_3H + H_2O \rightarrow m\text{-}NO_2C_6H_4OH + N_2 + H_2SO_4$$

Submitted by R. H. F. Manske.
Checked by H. T. Clarke and H. R. Brethen.

### 1. Procedure

In a 4-l. beaker is placed 210 g. of finely powdered *m*-nitroaniline (Note 1). A cold mixture of 450 cc. of water and 330 cc. of concentrated sulfuric acid is added with hand or mechanical stirring and then about 800 g. of finely crushed ice. When a homogeneous mixture has resulted, a solution of 105 g. of sodium nitrite in 250 cc. of water is added rapidly over a period of eight to ten minutes at the bottom of the mixture through a separatory funnel (Note 2) until a permanent color is given to starch-iodide paper (about 25–30 cc. of nitrite solution remains unused). The temperature during diazotization should be maintained at 0–5°. Stirring is continued for five to ten minutes longer and the solution allowed to settle for another five minutes. A heavy crystalline deposit of *m*-nitrobenzene diazonium sulfate settles at the bottom of the beaker, from which the supernatant liquid is decanted (Note 3).

While the diazotization is in progress 1 l. of concentrated sulfuric acid is added to 750 cc. of water in a 5-l. round-bottom flask and the mixture heated to boiling (160°) with a large ring burner. The liquor from the diazotization is then added from a separatory funnel at such a rate that the acid mixture boils very vigorously. About fifty minutes is required for this addi-

tion. The crystalline diazonium sulfate is then added in small portions at such a rate that the evolved nitrogen does not cause loss of material by excessive foaming. Boiling is continued for a few minutes longer and the contents of the flask are poured into a large beaker (Note 4) set in running cold water, and vigorously stirred to obtain a homogeneous crystal magma.

When completely cold, the nitrophenol is filtered, thoroughly pressed out, drained with suction, and washed with several portions of iced water, 450 cc. in all being used. It is spread on large sheets of filter paper and dried in a warm room. As thus prepared it has a yellowish brown appearance with darker particles intermixed. The yield is 170–180 g. (81–86 per cent of the theoretical amount) (Note 5).

It may be purified by recrystallization from hot hydrochloric acid, as recommended in Org. Syn. 3, 87, but on account of the difficulty of filtration this procedure is satisfactory on a small scale only. It is preferably distilled in 200-g. lots from a 500-cc. Claisen flask under 10–15 mm. pressure, b.p. 160–165°/12 mm. It is important that no air inlet be used to prevent bumping, since under these conditions it partly sublimes and causes trouble by stopping up the connections. A filter or distilling flask is used as a receiver and only a short but wide bore (10 mm.) air condenser is necessary. This product is pale yellow and melts at 95–96°. The yield from 200 g. of crude product is 180–185 g.

## 2. Notes

1. The *m*-nitroaniline used in these experiments was a commercial specimen of 98.4 per cent purity. A less pure specimen did not give a greatly decreased yield.

The *m*-nitroaniline may also be added to the mixture prepared by adding the ice to the diluted acid, but this procedure is not quite so satisfactory.

2. The addition of the sodium nitrite solution should be as rapid as possible. If added too rapidly, however, considerable foaming occurs.

3. The filtration of this solution is slow and usually unnecessary. Occasionally undetermined impurities are present and then washing of the diazonium salt with iced water by decantation, followed by filtration, becomes desirable.

4. In the first part of the addition the solution remains pale yellow to brown but when the solution becomes saturated with the nitrophenol the latter separates as a dark oil which is not filtered off. The final volume of the solution is about 3.5 l. and the boiling temperature about 120°.

5. By using the same molecular proportions the following *m*-nitrophenols were prepared in equally good yields from the corresponding *m*-nitroanilines: 3-methoxy-5-nitrophenol and 3-nitro-4,6-xylenol. In the former case it is advisable to use slightly more ice in the diazotization and add the diazonium solution to a mixture of equal volumes of sulfuric acid and water.

## 3. Methods of Preparation

*m*-Nitrophenol has recently been made in the laboratory of one of the editors by boiling *m*-nitrophenetole (from phenacetin by nitration, hydrolysis, and diazotization in alcohol) with hydrobromic acid, a method which is better than that given in Org. Syn. **3**, 87, but far inferior to the present method.

6. On increasing the scale of the preparation, the yield is somewhat higher.

### 3. Methods of Preparation

The method given is that of Böeseken and Bostet.[2] Phenylethylene has also been prepared by the addition of hydrobromic or hydriodic acid to cinnamic acid and subsequent treatment with alkali.[3] This method is stated to give higher yields but it requires more time and reagents. Phenylethylene has been prepared from phenylmethyl carbinol by distillation of the benzoic ester or by the action of phosphoric acid;[4] also by distilling $\beta$-phenylethyl phenyl acetate.[5] Phenylethylene may be prepared from ethyl benzene by pyrogenic decomposition,[6] or by conversion into phenyldibromoethane and treatment of the latter with magnesium.[7]

[1] Moureu and Dufraisse, Bull. soc. chim. (4), **31**, 225 (1922).

[2] Böeseken and Bastet, Rec. trav. chim. **32**, 190 (1913); Ostromislensky, U. S. pat. 1,541,176 [C. A. **20**, 424 (1926)].

[3] Fittig and Binder, Ann. **195**, 131 (1879).

[4] Klages and Allendorff, Ber. **31**, 1003, 1298 (1898).

[5] Hibbert and Burt, J. Am. Chem. Soc. **47**, 2240 (1925).

[6] Ostromislensky and Shepard, U. S. pat. 1,541,175 [C. A. **20**, 424 (1926)].

[7] v. Braun and Moldänke, Ber. **54**, 618 (1921).

# XXVI

## PHENYLSUCCINIC ACID

$$C_6H_5CH{=}C(CN)CO_2H + C_2H_5OH + HCl \rightarrow C_6H_5CH{=}C(CN)CO_2C_2H_5 + HCl + H_2O$$

$$C_6H_5CH{=}C(CN)CO_2C_2H_5 + NaCN + HCl \rightarrow C_6H_5CH(CN)CH(CN)CO_2C_2H_5 + NaCl$$

$$C_6H_5CH(CN)CH(CN)CO_2C_2H_5 + 5H_2O + 2HCl \rightarrow C_6H_5CH(CO_2H)CH_2CO_2H + C_2H_5OH + CO_2 + 2NH_4Cl$$

Submitted by ARTHUR LAPWORTH and WILSON BAKER.
Checked by J. B. CONANT and MILDRED EVANS.

### 1. Procedure

A. *Esterification of α-Cyano-β-Phenylacrylic Acid:*—In a 200-cc. round-bottom flask fitted with a reflux condenser, 50 g. of dry α-cyano-β-phenylacrylic acid (Org. Syn. 7, 20) is boiled for four and a half hours with 100 cc. of absolute alcohol containing 3–4 g. of anhydrous hydrogen chloride. The resulting solution is filtered rapidly while hot and allowed to stand overnight. Long, flat, colorless prisms separate which are filtered off with suction, washed with a little cold alcohol and dried in air. A further small quantity may be obtained by working up the mother liquor. The melting-point of the ethyl α-cyano-β-phenylacrylate is 50° and the yield 46.5–53 g. (82–94 per cent of the theoretical amount).

B. *Addition of Sodium Cyanide to Ethyl α-Cyano-β-phenylacrylate:*—Twenty grams of cyanophenylacrylic ester is treated with 40 cc. of 50 per cent alcohol and 10 g. of finely pow-

dered sodium cyanide. The mixture becomes warm and the ester rapidly dissolves, the reaction being completed by heating on the steam bath for two minutes. To this is added 200 cc. of water and the resulting clear, colorless solution of the addition product is decomposed with hydrochloric acid. This causes the precipitation of ethyl $\alpha$, $\beta$-dicyano-$\beta$-phenylpropionate as a yellowish oil, which on standing overnight and being stirred vigorously, or seeded if possible, sets to a yellowish solid mass. This is filtered off with suction and washed with cold water.

C. *Hydrolysis of Ethyl $\alpha$, $\beta$-Dicyano-$\beta$-phenyl Propionate:*— The product thus obtained is hydrolyzed by boiling under a reflux condenser for four hours with 80 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The substance goes into solution and this clear solution, on cooling, deposits phenylsuccinic acid in small crystals which are nearly colorless. These are filtered off, washed with cold water and dried. The yield of product melting at 164–166° is 17.6–18.4 g. (91–95 per cent of the theoretical amount based on the weight of ester used) (Notes 1 and 2).

## 2. Notes

1. The phenylsuccinic acid, if slightly off color, may be recrystallized easily from a hot water solution by rapid cooling. Five grams is dissolved in 400 cc. of hot water and then 60 cc. more of hot water is added. This solution is filtered and cooled in ice water with stirring until crystals separate. After standing the crystals are filtered off. The yield is 4.5 g. (90 per cent) of product melting at 167°.

2. The quantities of material used may be doubled from (B) on, in which case the refluxing in (C) requires at least a half hour longer for complete solution. One run with double quantities yielded 32.6 g.

## 3. Methods of Preparation

Phenylsuccinic acid has been prepared by the action of potassium cyanide and alcohol upon $\alpha$-chlorostyrene;[1] by the reaction

of ethoxyphenylmaleic anhydride and fuming hydriodic acid at 165°;[2] by the hydrolysis of phenylcyanopropionic acid, obtained by heating ethyl benzylidene malonate and aqueous potassium cyanide;[3] by the action of potassium cyanide on ethyl benzalmalonate and saponification of the product with potassium hydroxide;[4] by the addition of hydrogen cyanide to ethyl benzylidene acetoacetate in the presence of piperidine, followed by hydrolysis;[5] by the action of sulfuric acid on β-benzoyl-α-phenylpropionic acid oxime;[6] by the hydrolysis with hydrochloric acid of ethyl α, β-dicyano-β-phenylpropionate, obtained from sodium ethyl cyanoacetate and mandelonitrile;[7] by the hydrolysis of the addition product of hydrogen cyanide and ethyl-α-cyano-β-phenylacrylate.[8]

[1] Rügheimer, Ber. **14**, 428 (1881).
[2] Volhard and Henke, Ann. **282**, 83 (1894).
[3] Bredt and Kallen, Ann. **293**, 348 (1896).
[4] Wegscheider and Hecht, Monatsh. **24**, 417 (1903).
[5] Knoevenagel, Ber. **37**, 4069 (1904).
[6] Hann and Lapworth, J. Chem. Soc. **85**, 1365 (1904).
[7] Higson and Thorpe, J. Chem. Soc. **89**, 1471 (1906).
[8] Lapworth and McRae, J. Chem. Soc. **121**, 1704 (1922).

# XXVII

## PLATINUM CATALYST FOR REDUCTIONS

### (Platinic Oxide)

$$H_2PtCl_6 + 6NaNO_3 \rightarrow Pt(NO_3)_4 + 6NaCl + 2HNO_3$$

$$Pt(NO_3)_4 \rightarrow PtO_2 + 4NO_2 + O_2$$

$$PtO_2 + H_2O \rightarrow PtO_2 \cdot H_2O$$

Submitted by ROGER ADAMS, V. VOORHEES, and R. L. SHRINER.
Checked by HENRY GILMAN and S. A. HARRIS.

### 1. Procedure

IN a porcelain casserole (a Pyrex beaker may be used) is prepared a solution of 3.5 g. (Note 1) of a commercial C.P. chloroplatinic acid (Note 2) in 10 cc. of water and to this is added 35 g. of C.P. sodium nitrate (Note 3). The mixture is evaporated to dryness by heating gently over a Bunsen flame while stirring with a glass rod. The temperature is then raised, 350–370° being reached within about ten minutes. Fusion takes place, brown oxides of nitrogen are evolved, and a precipitate of brown platinum oxide gradually separates. During this procedure foaming often occurs, in which case the mass must be more vigorously stirred and an additional flame directed at the top of the reaction mixture. If the burner under the casserole is removed when foaming starts, the top of the fused mass solidifies and foaming may become sufficient to carry material over the sides of the casserole. By the end of fifteen minutes, when the temperature has reached about 400°, the evolution of gas has greatly decreased. At the end of twenty minutes the temperature should be 500–550°. At this point the vigorous evolution

of oxides of nitrogen has practically ceased and a gentle evolution of gas takes place. The temperature is held at this point (best with the full force of the burner directly on the casserole) until about thirty minutes have elapsed, when the fusion should be complete. This temperature (500–550°) is most satisfactory for the fusion (Note 4) in order to obtain a catalyst of maximum activity and minimum lag (Note 5). The temperature indicated is generally attained in this laboratory by the use of one ordinary Bunsen burner turned on as high as possible; where the gas pressure is lower a Meker burner may be necessary. The mass is allowed to cool and is then treated with 50 cc. of water. The brown precipitate settles to the bottom and can be washed by decantation once or twice, then filtered (preferably through a hardened filter paper on a Gooch crucible) and washed on the filter until practically free from nitrates. If the fusion has been properly carried out no difficulty is encountered in this procedure; but if the temperature of fusion has not been high enough or has not been maintained for a sufficiently long time the precipitate tends to become colloidal on addition of water and does not filter well; moreover under these conditions, the yield of product and its activity as a catalyst are diminished. Sometimes the precipitate becomes colloidal only when practically all of the nitrates are removed; in this case it is better to stop washing as soon as the colloid starts to form, since small traces of the salt do not affect the efficiency of the catalyst. The filtrates should be tested for platinum and saved if any is present (Note 6). The oxide is either used directly, or more generally it is dried in a desiccator and portions of the dried material weighed out for reductions. The yield is 1.57–1.65 g. (95–100 per cent of the theoretical amount) (Notes 4 and 7). The use of platinum oxide is illustrated in the reduction of ethyl *p*-nitrobenzoate to ethyl *p*-aminobenzoate (p. 66) and of benzalacetophenone to benzylacetophenone (p. 36).

The platinum black by reduction of the oxide may sometimes be used a second, third or even more times in the reduction of certain compounds merely by reactivating (Note 8) with air or oxygen. A spent catalyst must be reworked (Note 9)

along with the platinum recovered from filtrates (Note 6), filter papers (Note 10) and the casserole (Note 11). In the use of platinum-oxide platinum black for reductions, certain types of compounds require different physical conditions from others in order to obtain the best results in each case and factors such as the following must be taken into consideration: the temperature, the medium in which the reduction of platinum oxide to platinum black occurs (Note 12), the effect of traces of inorganic salts (Note 13), the solvent employed (Note 14). Palladous-oxide palladium black has been used for catalytic reduction, and in some cases has proved a more efficient catalyst than the platinum-oxide platinum black though generally this has not been found true (Note 15).

## 2. Notes

1. If a considerable quantity of platinum oxide is desired it is more satisfactory to prepare several runs of the size indicated than one large run, since spattering and the evolution of gases make large amounts inconvenient to handle. The activity of the catalyst appeared in certain cases to decrease after standing for several weeks and therefore the oxide should preferably be prepared as required.

2. Commercial C.P. chloroplatinic acid varies somewhat in its purity. In this work that from the Mallinckrodt Chemical Works, St. Louis, was used and gave very satisfactory results. Since small amounts of impurities in the catalyst are important factors in the rate of reduction of certain types of compounds, this question of impurities in the chloroplatinic acid must be taken into account (Note 13). In a large proportion of the reductions studied, platinum oxide prepared from the chloroplatinic acid mentioned gave as good results as that from spectroscopically pure chloroplatinic acid made according to the directions of Wichers.[1]

If only platinum metal is available this is dissolved in aqua regia and evaporated to dryness several times with hydrochloric acid, until free from nitrates (Note 9) and the product purified according to the method of Wichers.

3. U.S.P. sodium nitrate could probably be used in place of the C.P. grade in most instances, but in one type of reduction at least (that of aminophenols to cyclic amino alcohols) the small amount of impurities in the U.S.P. grade affected the activity of the catalyst.

4. The relation of temperature of fusion to the properties of the catalyst produced was determined[3c] by carrying out the fusion at various temperatures which were recorded by stirring continuously with a thermocouple encased in a Pyrex glass tube, and reading the temperature on a pyrometer. The product prepared at lower temperatures is usually light brown in color and has a greater tendency to become colloidal on washing. The catalyst prepared at intermediate temperatures is brown in color and at 600° has a very deep brown color. The color may vary even when the catalyst is prepared under conditions which are essentially the same, but if the temperature indicated in the procedure is used the oxide will be satisfactory.

The products prepared at temperatures below 450° and above 600° have a lower activity and require a greater length of time for reduction to platinum black than those prepared at temperatures between 450° and 600°.

If the fusion temperature is about 300°, the yield of platinum oxide is very low, at higher temperatures the yield increases, and at temperatures of 450° and higher it is practically quantitative. With a proper fusion a slightly lower yield than quantitative is generally not due to non-precipitation of the platinum but to loss by spattering and to deposition of a small amount on the casserole.

5. The brown oxide is a heavy granular powder which settles to the bottom of the solution in the bottle in which the reduction is carried out (p. 10). It must be reduced to platinum black before it becomes a catalyst for the reduction. When the hydrogen is admitted and the bottle shaken the brown oxide becomes black and whips up into a fine suspension. The time necessary for the change of the oxide to platinum black is called the lag. The time of lag varies usually from several seconds to two or three minutes, depending upon the conditions under which

the platinum oxide is reduced to platinum black. In general the lag is short provided the reduction of the oxide is carried out merely in the presence of solvent; if carried out in the presence of solvent and substance to be reduced, as is more frequently the case, the character of the substance being reduced has a considerable effect, and sometimes a lag of ten to fifteen minutes occurs. In experiments where foreign salts are added as promoters or poisons the lag varies widely, though generally within a maximum of ten to fifteen minutes; exceptions occur and it was found that the lag was forty to sixty minutes more when the platinum oxide was reduced in the presence of a little sodium nitrite and an alcoholic solution of benzaldehyde. It is probable also that the temperature at which the platinum oxide is formed from the chloroplatinic acid and the solvent present have some effect on the ease with which it is reduced to platinum black.

6. It is advisable to test for platinum in all the filtrates before discarding any of them, since there is sometimes a tendency for small amounts of platinum to remain in solution. A very satisfactory and delicate test for platinum, described by Wöhler,[2] consists in making the solution acid with hydrochloric acid and adding a few drops of stannous chloride. A yellow color develops when platinum is present and a brown color when it is in large amount. If any doubt exists as to whether or not the solution is yellow, it should be shaken with a small amount of ether; the yellow color concentrates in the ether layer, indicating the presence of platinum. From the sodium nitrate filtrates a large proportion of the platinum can be recovered by adding excess of formaldehyde and sodium hydroxide and heating. Upon standing, platinum black separates and may be filtered and worked up with other platinum black residues. The platinum which still remains in solution after this precipitation can be recovered by acidifying the solution and heating with zinc.

7. Quantitative analyses show the oxide to be $PtO_2 . H_2O$.[3c] It usually contains a very small amount of glaze from the casserole, but this does not affect its use or activity. The oxide

dissolves only slightly in hot aqua regia even after long heating; it is insoluble in boiling concentrated nitric acid and only slightly, or at least only slowly, soluble in boiling concentrated hydrochloric acid. Constant-boiling hydrobromic acid, on the other hand, dissolves it completely in the cold with the evolution of bromine and the formation of a solution of bromoplatinic acid from which the red potassium salt can be readily precipitated or the solution may be evaporated and the residue used directly in a subsequent fusion.

8. The platinum-oxide platinum black, like any other platinum black, gradually loses its activity with use. In the reduction of certain types of compounds, notably aldehydes the catalyst can be revivified by shaking with air or oxygen for a few minutes.[3b] Frequently this must be done in order to have the reduction go to completion and often it is desirable to do so during a reduction so as to increase the rate of reaction. In other reductions attempted reactivation as described results in the complete inactivation and frequently the coagulation of the catalyst. In reducing certain substances, the catalyst tends to coagulate in lumps during the reduction, particularly toward the end of the reduction. In these instances reworking of catalyst is necessary (Note 9) before it can be used satisfactorily for a second run. On the other hand in the reduction of many substances, the catalyst does not coagulate, but after the reduction is complete it gradually settles if allowed to stand, and the supernatant liquid may be decanted; when a second run is made with this catalyst it is frequently not much inferior to new catalyst and forms a fine suspension as soon as shaking is again started.

9. Platinum residues may be reworked by dissolving them in aqua regia, filtering, evaporating the filtrate to dryness, taking up with a little water and fusing with sodium nitrate. If organic matter is present in the chloroplatinic acid, as is generally the case when recovered platinum is used, it will be oxidized during the fusion and, excepting in cases requiring a spectroscopically pure platinum, seems to have no deleterious effect. Repeated

reworking does seem to cause an accumulation of poison in the catalyst and under these conditions it should be purified as described by Wichers.[1]

10. There is always a certain amount of the oxide which adheres to the filter paper during filtration, so that these papers should be ignited and the residue added to any platinum catalyst which has already become inactive and requires redissolving and reprecipitation (Note 9).

11. The thin film of oxide which remains in the casserole is dissolved by treating with a little constant-boiling hydrobromic acid (Note 7); the solution obtained may then be evaporated and the residue added to the next fusion mixture.

12. In certain reductions it is an advantage to reduce the platinum oxide to platinum black by shaking with hydrogen in the presence of solvent only, before the substance to be reduced is added to the mixture. More often the catalyst is reduced in the presence of the substance to be reduced; with aldehydes for example the platinum black is usually more finely divided and generally more active if prepared in presence of the aldehyde.

13. Certain inorganic salts have the effect of promoting or retarding the action of the catalyst.[3 b, d, e, g, h, i, j, k, l] Thus in the reduction of aldehydes, iron salts in mere traces have a remarkable effect in increasing the rate of reduction and in inhibiting the tendency of the catalyst to lose its activity. To a lesser extent manganese, nickel, and other salts have the same effect. On the other hand, with the majority of substances studied, the effect of these salts is to retard the reduction.

14. The solvent used is an important factor influencing the rate of reduction[3e] and no generalization can be made beyond the one that alcohol, either 95 per cent or absolute has proved to be the best solvent for most of the compounds thus far studied. Ethyl acetate and glacial acetic acid may be used to advantage in some cases.

15. Palladous oxide,[3f] PdO, may be prepared by the fusion of palladous chloride with sodium nitrate, and is an effective catalyst in hydrogenation, the most active form being produced when the fusion temperature is 600°.

### 3. Methods of Preparation

Platinic oxide has been prepared previously by the interaction of platinic chloride and excess sodium hydroxide.[4] Since the catalyst itself is platinum black, the other methods for its preparation are given below.

Platinum black has been prepared chiefly by the reduction of chloroplatinic acid with formaldehyde;[5] the details have been improved by Willstätter and Hatt;[6] Willstätter and Waldschmidt-Leitz,[7] and by Feulgen.[8]

[1] Wichers, J. Am. Chem. Soc. **43**, 1268 (1921).

[2] Wöhler, Chem. Ztg. **31**, 938 (1907).

[3] Articles in this field are (*a*) Voorhees and Adams, J. Am. Chem. Soc. **44**, 1397 (1922); (*b*) Carothers and Adams, **45**, 1071 (1923); (*c*) Adams and Shriner, **45**, 2171 (1923); (*d*) Kaufmann and Adams, **45**, 3029 (1923); (*e*) Carothers and Adams, **46**, 1675 (1924); (*f*) Shriner and Adams, **46**, 1683 (1924); (*g*) Carothers and Adams, **47**, 1047 (1925); (*h*) Pierce and Adams, **47**, 1098 (1925); (*i*) Kern, Shriner and Adams, **47**, 1147 (1925); (*j*) Heckel and Adams, **47**, 1712 (1925); (*k*) Tuley and Adams, **47**, 3061 (1925); (*l*) Adams and Garvey, **48**, 477 (1926); (*m*) Hiers and Adams, Ber. **59**, 162 (1926); (*n*) Adams, Cohen and Rees, J. Am. Chem. Soc. **49**, 1093 (1927); (*o*) Hiers and Adams, **49**, 1099 (1927); (*p*) Carothers and Jones, **47**, 3051 (1925). A study of ketones as yet unpublished has indicated that reductions are more satisfactory when no solvent is used.

[4] Wöhler, Z. anorg. Chem. **40**, 434 (1904); Bellucci, Z. anorg. Chem. **44**, 171 (1905); Wöhler and Frey, Z. Elektrochem. **15**, 132 (1909).

[5] Loew, Ber. **23**, 289 (1890).

[6] Willstätter and Hatt, Ber. **45**, 1472 (1912).

[7] Willstätter and Waldschmidt-Leitz, Ber. **54**, 113 (1921).

[8] Feulgen, Ber. **54**, 360 (1921).

# XXVIII

## SODIUM *p*-ARSONO-N-PHENYLGLYCINAMIDE

### (Tryparsamide)

$$p\text{-}H_2O_3AsC_6H_4NH_2 + ClCH_2CONH_2 + NaOH \rightarrow p\text{-}H_2O_3AsC_6H_4NHCH_2CONH_2 + NaCl + H_2O$$

$$p\text{-}H_2O_3AsC_6H_4NHCH_2CONH_2 + 2NaOH \rightarrow p\text{-}Na_2O_3AsC_6H_4NHCH_2CONH_2 + 2H_2O$$

Submitted by W. A. JACOBS and M. HEIDELBERGER.
Checked by ROGER ADAMS and L. F. MARTIN.

### 1. Procedure

To a solution of 130 g. (0.6 mole) of arsanilic acid (Org. Syn. 3, 13) in 600 cc. (0.6 mole) of normal sodium hydroxide is added 52 g. (0.62 mole) of sodium bicarbonate and 70 g. (0.75 mole) of chloroacetamide (Org. Syn. 7, 16). The mixture is heated on a water bath to 90–100° and a steady evolution of carbon dioxide occurs. At the end of two hours, when gas evolution has practically ceased, the mixture is cooled to 40° C., stirred vigorously and 150 cc. of 1 : 1 hydrochloric acid poured in rapidly. *p*-Arsonophenylglycinamide crystallizes at once and, after cooling to room temperature, is filtered by suction and washed once with 2 per cent hydrochloric acid (Note 1), then with cold water. The crude product thus obtained is contaminated with some arsanilic acid and possibly other products. These are removed during purification. The crude product is suspended in about 400 cc. of water and with vigorous stirring, treated carefully with 25 per cent aqueous sodium hydroxide until solution is just complete. At this point the mixture is still acid to litmus and an excess of sodium hydroxide is to be avoided to prevent decomposition of the product. About 15 g. of boneblack

is added, the mixture stirred for five minutes without heating and filtered. The filtrate is treated during vigorous stirring with 100 cc. of 1 : 1 hydrochloric acid and the pure acid at once separates. After cooling, it is filtered by suction and washed thoroughly with small portions of ice-cold water until the filtrate is practically halogen-free (Note 2).

The acid, without drying, is suspended in about 200 cc. of distilled water and with vigorous stirring, cautiously (Note 3) treated with 25 per cent sodium hydroxide solution until dissolved and the solution reacts neutral to litmus. The solution is then filtered through folded filter paper which should be free from soluble calcium salts, otherwise the filtrate will remain clouded by a suspension of the calcium salt. The clear, faintly yellow or colorless filtrate is then vigorously stirred and treated with 1.5 volumes of 95 per cent alcohol. Crystallization is induced by rubbing with a rod and then an additional volume of alcohol is added. The mixture should be allowed to cool to about 20° and stand for at least two hours to complete the precipitation of the salt, which is then filtered by suction and washed thoroughly with 85 per cent alcohol. The salt is then air-dried. The yield is 73–77 g. (38–40 per cent of the theoretical amount).

## 2. Notes

1. From this filtrate approximately 15–30 g. of arsanilic acid may be recovered by just neutralizing to Congo Red with sodium hydroxide.

2. If the free acid is desired it may be obtained by drying the product at this stage. The yield of free acid is about 100 g. (60 per cent of the theoretical amount).

3. If sodium hydroxide is added too rapidly some solid precipitates which does not redissolve.

## 3. Methods of Preparation

This procedure for the preparation of tryparsamide has been described in the literature.[1]

[1] Jacobs and Heidelberger, J. Am. Chem. Soc. **41**, 1590 (1919); U. S. pat. 1,280,119 [C.A. **12**, 2058 (1918)].

# XXIX

# STYRENE OXIDE

$$C_6H_5CH=CH_2+C_6H_5COO_2H \rightarrow C_6H_5\underset{\diagdown O \diagup}{CH—CH_2}+C_6H_5CO_2H$$

Submitted by HAROLD HIBBERT and PAULINE BURT.
Checked by ROGER ADAMS and F. E. KENDALL.

## 1. Procedure

To a solution of 42 g. (0.33 mole) of benzoylhydroperoxide (p. 30) in 500 cc. of chloroform is added 30 g. (0.3 mole) of styrene (b.p. 141–143°) (p. 84). The solution is kept at 0° for twenty-four hours and is shaken frequently during the first hour. At the end of twenty-four hours, titration of an aliquot part of the solution shows that only the excess of benzoylhydroperoxide remains (Note 1).

The benzoic acid is removed from the chloroform solution by shaking with an excess of 10 per cent sodium hydroxide solution, the alkali is removed by washing with water, and the chloroform solution is dried with anhydrous sodium sulfate. It is then fractionated through an efficient distilling column (Org. Syn. 1, 40). Removal of the chloroform leaves a practically colorless liquid which distils at 188–192° (uncorr.) (Note 2). The yield is 24–26 g. (70–75 per cent of the theoretical amount).

## 2. Notes

1. The benzoylhydroperoxide may be analyzed by mixing with an excess of acidified potassium iodide and titrating the liberated iodine with sodium thiosul ate (p. 31).

2. If the styrene oxide is distilled over a free flame some

decomposition takes place, indicated by the formation of water. This is not observed if the product is distilled from an oil bath.

## 3. Methods of Preparation

Styrene oxide has previously been prepared by the action of iodine, water and mercuric oxide on styrene.[1] A description of Hibbert's method[2] using benzoylhydroperoxide has appeared in the literature.

[1] Fourneau and Tiffeneau, Compt. rend. **140**, 1596 (1905).

[2] Hibbert and Burt, J. Am. Chem. Soc. **47**, 2240 (1925).

## XXX

# TRIMETHYLACETIC ACID

$$(CH_3)_3CCl + Mg \rightarrow (CH_3)_3CMgCl$$

$$(CH_3)_3CMgCl + CO_2 \rightarrow (CH_3)_3CCO_2MgCl$$

$$(CH_3)_3CCO_2MgCl + H_2O \rightarrow (CH_3)_3CCO_2H + MgOHCl$$

Submitted by S. V. PUNTAMBEKER and E. A. ZOELLNER.
Checked by J. B. CONANT and A. HAROLD BLATT.

## 1. Procedure

IN a 3-l., three-neck, round-bottom flask, fitted with a mechanical stirrer and mercury seal, a 500-cc. separatory funnel and an efficient reflux condenser, is placed 61 g. (2.5 moles) of magnesium turnings or powder (Note 1). The magnesium is then covered with 200 cc. of anhydrous ether. Five cc. of pure *tert*-butyl chloride (with a crystal or two of iodine) is added to start the reaction. Stirring is begun and a solution of 227 g. (2.5 moles) of pure *tert*-butyl chloride (p. 50) in 1100 cc. of anhydrous ether is dropped slowly (Note 2) on the magnesium during six to eight hours. The reaction is practically complete when all the halide has been added, but stirring should be continued for fifteen minutes longer.

The reaction mixture is now surrounded by an ice and salt mixture. The separatory funnel is replaced by a two-hole rubber stopper containing a thermometer (bulb immersed in the reaction mixture) and a glass tube the outer end of which is connected to a mercury trap (Note 3). When the temperature of the reaction mixture has fallen to 0°, the condenser is replaced by a tube 10 mm. in diameter and adjusted so the end is 50 mm. above the surface of the reaction mixture. The reaction mix-

ture is stirred and carbon dioxide is added through this tube directly from a cylinder after passing through two bottles containing concentrated sulfuric acid. The carbon dioxide is added as rapidly as it is used up. The temperature is controlled by the rate of stirring and should not go above +8°. After two and one-half to three hours the temperature falls below 0°. Then the addition is continued for one-half hour under a pressure of 45 mm. (Note 3). The temperature falls to −3° to −5° at the end of this time and the reaction is complete.

After surrounding the flask with ice, the reaction mixture is hydrolyzed (Note 4) with 25 per cent sulfuric acid. The reaction mixture is transferred to a 2-l. separatory funnel and the ether layer separated (Note 4). The water layer is extracted with four 100-cc. portions of ether. The combined ether extracts are then washed with four 100-cc. portions of 25 per cent sodium hydroxide solution to remove the trimethylacetic acid from the ether.

The aqueous alkaline extract is heated to 100° to remove ether and volatile impurities. The solution is then cooled with ice and acidified with 25 per cent sulfuric acid, and the organic acid separated. The water layer is distilled from a 2-l. flask until no more oily solution comes over. The distillate is saturated with salt and the acid layer is separated. This water layer together with the low boiling fraction from distillation of the crude trimethylacetic acid is distilled and the distillate salted out as before.

The combined acid layers are distilled from a 250-cc. Claisen flask connected to an air condenser, which in turn is connected to a side-arm flask cooled by running water. The trimethylacetic acid is collected at 162–165°/atm. press., 110–112/124 mm. The yield, which depends somewhat on the form of magnesium, is 157–162 g. (61–63 per cent of the theoretical amount based on *tert*-butyl chloride) when ordinary magnesium turnings are used and 177–178 g. (69–70 per cent) when 200-mesh magnesium powder is used. The acid melts at 34–35°.

## 2. Notes

1. The yield of product depends to a considerable extent upon the form of magnesium used. Either the finer commercial grade of turnings should be used or the 30 to 200-mesh powdered magnesium that is kept in a tightly stoppered bottle when not in use. The powdered magnesium makes possible a 5–8 per cent increase in yield.

2. The rate of addition of the halide solution is important. The slower the rate the better the yield. A delivery constant should be determined of the separatory funnel so that the solution can be added uniformly over a period of six to eight hours.

3. The mercury trap enables the operator to adjust the flow of the carbon dioxide according to the rate of absorption, and to apply a pressure of 45 mm. during the last half-hour. The pressure itself has practically no effect. The trap consists merely of a narrow glass test-tube containing mercury, and the tube is made to extend beneath the surface.

4. The hydrolysis of the reaction mixture and subsequent separation of the acid is the procedure given by Gilman and Parker (Org. Syn. **5**, 25). Sulfuric acid should be added during the hydrolysis as long as any particles of magnesium are present. The water layer does not become clear, due to solidification of the organic acid.

## 3. Other Methods of Preparation

See p. 110.

XXXI

## TRIMETHYLACETIC ACID

$$(CH_3)_3CCOCH_3 + 4NaOH + 3Br_2 \rightarrow (CH_3)_3CCO_2Na + 3H_2O + CHBr_3 + 3NaBr$$

$$(CH_3)_3CCO_2Na + H_2SO_4 \rightarrow (CH_3)_3CCO_2H + NaHSO_4$$

Submitted by L. T. SANDBORN and E. W. BOUSQUET.
Checked by F. C. WHITMORE and T. OTTERBACHER.

### 1. Procedure

IN a 5-l. round-bottom flask fitted with a mechanical stirrer is placed a solution of 330 g. (8 moles) of stick sodium hydroxide (U.S.P.) in 2.8 l. of water and the solution is cooled to 0° in an ice-salt bath. To the well-stirred solution 480 g. (3 moles) of bromine is added from a separatory funnel at such a rate as to keep the temperature below 10° (Note 1) (fifteen to twenty minutes). The solution is cooled again to 0° and 100 g. (1 mole) of pinacolone (Org. Syn. **5**, 91) is added from a separatory funnel, keeping the temperature below 10°. After the solution is decolorized (about an hour) it is stirred for three hours at room temperature.

The flask is then fitted with a separatory funnel and a con denser for distillation, and heated with a Meker burner to steam distil the bromoform and carbon tetrabromide (Notes 2 and 3).

The burner is then removed, the mixture is cooled to 50°, and 400 cc. of concentrated sulfuric acid (Note 4) is added through the separatory funnel. The heat of neutralization causes some trimethylacetic acid to distil with water. When all the acid is added the flask is heated again and the trimethylacetic acid comes over with about 400 cc. of water. When

all of the trimethylacetic acid (70–80 cc.) has distilled, a liquid heavier than water begins to come over. The distillation is stopped and the acid separated from the water in a separatory funnel and dried either with calcium chloride or by distilling with benzene which carries over all water (Note 5). The trimethylacetic acid is further purified by distillation under reduced pressure. It boils at 75–78°/20 mm. and the yield is 63–65 g., melting at 34–35°.

The water layer is extracted with two 100-cc. portions of ether. The combined ether solutions are dried with calcium chloride, the ether distilled, and the residue fractionated under reduced pressure, using a modified Claisen flask (Org. Syn. 1, 40). Ten to twelve grams may be obtained in this way. The total yield is 72–75 g. (71–74 per cent of the theoretical amount).

## 2. Notes

1. The temperature must be kept low during the reaction to prevent formation of sodium bromate.

2. The reaction between sodium hydroxide and tribromopinacolone is not complete at room temperature. Heating in this manner, rather than separation in the cold, results in an increase of 10–15 per cent in the yield.

3. The bromoform passes over with the steam rather rapidly. In some runs some carbon tetrabromide was also obtained. Toward the end of the steam distillation a heavy oil that is more or less of a lachrymator may come over. This is undoubtedly brominated pinacolone. The bromoform may be purified by vacuum distillation. One run gave 115 g. of product, boiling at 78–79°/22 mm.

4. An equivalent amount of hydrochloric acid may be used without affecting the yield.

5. The trimethylacetic acid is dried very easily by distilling with about 50 cc. of benzene at ordinary pressure until all of the water is removed and then the residue is distilled under reduced pressure.

### 3. Methods of Preparation

Trimethylacetic acid may be made by the hydrolysis of *tert*-butyl cyanide with weak hydrochloric acid at 100°.[1] It is also obtained by oxidation of trimethylpyroracemic acid with silver oxide or potassium dichromate and sulfuric acid,[2] by oxidation of *tert*-butylethylene with permanganate solution,[3] or by oxidation of dimethyl 2,2-propanol with chromic acid.[4] Schroeter reports the formation of trimethylacetic acid by rearrangement of the oxime of trimethylacetophenone to give the anilide of trimethylacetic acid, which can be hydrolyzed to give the acid.[5]

The method given in these directions [6] may be modified by using potassium hypochlorite [7] or chromic acid [8] as the oxidizing agent.

The directions given in Exp. XXX by the reaction of *tert*-butyl magnesium chloride and carbon dioxide are an improvement on those described by Bouveault.[9]

[1] Butlerow, Ann. **165**, 322 (1873).
[2] Glücksmann, Monatsh. **10**, 777 (1889).
[3] Fomin and Sochanski, Ber. **46**, 247 (1913).
[4] Franke, Monatsh. **34**, 1900 (1913).
[5] Schroeter, Ber. **44**, 1206 (1911).
[6] Richard and Langlais, Bull. soc. chim. (4) **7**, 464 (1910).
[7] Böeseken, Rec. trav. chim. **29**, 99 (1910).
[8] Friedel and Silva, Ber. **6**, 146, 826 (1873).
[9] Bouveault, Compt. rend. **138**, 1108 (1904).

XXXII

## TRIMETHYLENE CHLOROHYDRIN

$$HOCH_2CH_2CH_2OH + HCl \rightarrow ClCH_2CH_2CH_2OH + H_2O$$

Submitted by C. S. Marvel and H. O. Calvery.
Checked by H. T. Clarke and M. R. Brethen.

### 1. Procedure

A 100-cc. round-bottom wide-mouth flask (or a large test-tube 18 cm. long and 4.5 cm. wide) is fitted with a rubber stopper carrying a separatory funnel, a thermometer, an inlet tube reaching almost to the bottom of the flask and an outlet tube leading to a condenser set for downward distillation. A receiver consisting of a suction flask is attached tightly to the end of the condenser and the side arm of the receiver is attached to a reflux condenser. A tube is led from the top of the condenser to the hood in order to take care of excess hydrogen chloride during the distillation, or better the apparatus described in Note 2, p. 27, is used. About 25–30 cc. of trimethylene glycol (b.p. 210–215°) is placed in the flask and heated by means of an oil or metal bath to 150–170°. A *very* rapid stream of dry hydrogen chloride (Note 1) is now led into the hot glycol through the inlet tube. A reddish distillate consisting of water, trimethylene chlorohydrin, hydrogen chloride and some unchanged glycol begins to distil. As rapidly as the glycol is used up in the reaction flask, more is added from the separatory funnel. It is always advisable to keep the amount of material in the reaction flask as small as possible. The rate at which the hydrogen chloride is passed through the flask controls the reaction and also has a marked effect on the yield (Note 2). The best results are obtained by passing in the gas rapidly enough

to use up 2–3 cc. of trimethylene glycol in one minute. The process is continuous and can be run indefinitely without changing the apparatus. The weight of crude distillate from 1800 g. of trimethylene glycol is usually 2300–2500 g.

To obtain the trimethylene chlorohydrin, the distillate from this operation is heated for about one hour on a steam bath in order to drive out most of the excess hydrogen chloride. The distillate is then fractionated under reduced pressure (Note 3) in a modified Claisen flask (Org. Syn. 1, 40). The fractionating side arm should be 25 cm. in length. The fractions collected under 10 mm. are: to 55°, 55–57°, 57–65°, 65–85°, 85–105°, residue.

Before a further fractionation is carried out, the residue is discarded; the portion boiling at 85–105°, consisting chiefly of unchanged trimethylene glycol, is set aside for use in a later preparation; the low-boiling portion up to 55° consisting mainly of water and hydrogen chloride with some trimethylene chloride (Note 4) and trimethylene chlorohydrin, is neutralized carefully with powdered sodium carbonate. Two layers form and the upper containing the chlorohydrin is separated, dried over anhydrous potassium carbonate and again replaced as the portion boiling up to 55°. Another complete fractional distillation, carried out in the usual way, is now made except that the highest fraction boils at 65–85°/10 mm.

The material boiling above 65°/10 mm. is chiefly trimethylene glycol and is used in a succeeding experiment. The final yield of trimethylene chlorohydrin (Note 5) boiling at 60–64°/10 mm. is 835–1000 g. from 1800 g. of trimethylene glycol (50–60 per cent of the theoretical amount), and 400–450 g. of trimethylene glycol is recovered.

## 2. Notes

1. The hydrogen chloride may be generated by any method desired. Since a large quantity of gas is required, the procedure described (Org. Syn. 2, 29) is rather expensive. A more satisfactory arrangement is to half fill a 12-l. flask with a paste of salt and concentrated hydrochloric acid and run into this com-

mercial sulfuric acid. The gas is dried by a single wash bottle of sulfuric acid.

If sulfuric and hydrochloric acids are used then for the conversion of 1800 g. of trimethylene glycol, a 20-l. bottle half-filled with concentrated sulfuric acid is treated with concentrated hydrochloric acid introduced through a tube reaching to the bottom. The hydrochloric acid is added at the rate of 30–40 drops per minute. Two charges of sulfuric acid are needed and a total of about 24 kg. of hydrochloric acid.

2. The yield of chlorohydrin is largely determined by the rate at which the reaction is carried out. A very rapid stream of hydrogen chloride is absolutely essential for obtaining the yields mentioned. Moreover, it is very important to keep as small an amount of glycol as possible in the reaction flask. If larger amounts of glycol are present at any one time, the yield of product is lowered and considerable tar is produced.

3. Trimethylene chlorohydrin cannot be distilled under atmospheric pressure without some decomposition. The fractionation can be carried out at ordinary pressures when the fractions collected are up to 125°, 125–158°, 158–164°, 164–190°, 190–210° and residue. This procedure is less desirable as some hydrogen chloride is evolved and the product turns dark on standing.

4. The portion boiling up to 55°/10 mm., obtained after the second fractionation, was washed with concentrated sulfuric acid, then water, and finally dried and distilled. A certain amount of trimethylene chloride was sometimes obtained, boiling at 115–120° and amounting to about 30 per cent of the total fraction.

5. The chlorohydrin contains a very small amount (less than 0.5 per cent) of water-insoluble material, which is probably trimethylene chloride and di-$\gamma$-chloropropyl ether.

### 3. Methods of Preparation

Trimethylene chlorohydrin has been prepared from trimethylene glycol by the action of dry hydrogen chloride

under various conditions;[1] by the action of aqueous hydrochloric acid;[2] and by the action of sulfur chloride.[3] It has also been prepared from $\gamma$-chloropropyl acetate and methyl alcoholic hydrochloric acid.[4]

[1] Reboul, Ann. chim. phys. (5) **14**, 493 (1878); Malengreau and Lebailly, Z. physiol. Chem. **67**, 37 (1910); Karvonen, Ann. acad. sci. Fennicae [A], **3**, 1 (1912) [Chem. Zentr. **1912**, II, 1271]; Derick and Bissell, J. Am. Chem. Soc. **38**, 2481 (1916); Karvonen, Ann. acad. sci. Fennicae [A], **5**, 1 (1914) [C.A. **14**, 2176 (1920)].

[2] Norris and Mulliken, J. Am. Chem. Soc. **42**, 2095 (1920); Hultman, Davis, and Clarke, J. Am. Chem. Soc. **43**, 369 (1921).

[3] Derick and Bissell, J. Am. Chem. Soc. **38**, 2481 (1916).

[4] Henry, Bull. Acad. roy. Belg. cl. sci. **8**, 738 (1906).

## XXXIII

## TRIPHENYLAMINE

$$2(C_6H_5)_2NH + 2C_6H_5I + K_2CO_3 \rightarrow 2(C_6H_5)_3N + 2KI + H_2O + CO_2$$

Submitted by F. D. HAGER.
Checked by HENRY GILMAN and R. McCRACKEN.

### 1. Procedure

IN a 2-l. three-neck, round-bottom flask, fitted with a very efficient mechanical stirrer, a 100-cc. separatory funnel and a large air-cooled reflux condenser (Note 1), the upper part of which is bent downwards and attached to a vertical water condenser, are placed 176 g. (1.04 moles) of ground diphenylamine (Note 2), 204 g. (1 mole) of iodobenzene, 1 l. of nitrobenzene (Note 3), 138 g. (1 mole) of finely powdered anhydrous potassium carbonate and 5 g. of copper powder (Note 4).

The reaction mixture is then stirred very vigorously and boiled at such a rate that the nitrobenzene condenses in the upper third of the air-cooled reflux condenser and flows back in an almost steady stream. The water formed in the reaction passes over, together with a small amount of nitrobenzene and iodobenzene, and is condensed by the water-cooled condenser. This distillate is freed of water by shaking with a small quantity of sodium sulfate and returned at intervals through the separatory funnel to the reaction flask. Heating is continued for about twenty-four hours or until the reaction is complete, as is evidenced by the non-evolution of water (Note 5).

The reaction mixture is allowed to cool somewhat and is then transferred to a 5-l. flask, and the nitrobenzene together with a little of the excess diphenylamine is removed by steam distillation. During distillation the flask should be heated to

prevent excessive condensation of steam (Note 6). Steam distillation should be continued until a liter of distillate contains less than 5 cc. of water-insoluble material (Note 7).

The reaction mixture is cooled and the crude amines which separate are collected on a suction funnel and washed twice with 400-cc. portions of water. The filtrate and washings should be saved for the recovery of iodine (Note 8). The precipitate on the funnel is transferred to a 2-l. beaker, dissolved in about 1 l. of benzene, filtered, and the benzene-insoluble part washed three times with 75-cc. portions of benzene. The benzene solution and washings are combined and separated mechanically from as much water as is possible. The water is then completely removed by distilling until the distillate comes over clear. If necessary, dry benzene is added to the solution in order to have a final volume of about 1200 cc.

When the water is entirely removed, the benzene solution is cooled and an excess of dry hydrogen chloride is passed into it to precipitate the diphenylamine as the hydrochloride (Note 9).

After standing about three hours, the diphenylamine hydrochloride is filtered and washed with benzene (Note 10). The benzene is distilled from the filtrate (Note 11) and the residual triphenylamine is transferred to a 500-cc. modified Claisen flask (Org. Syn. 1, 40) and distilled under reduced pressure. The first fraction consists of some benzene, then the temperature rises rapidly and a few cubic centimeters of deeply colored distillate comes over just before the amine fraction, which is collected at 195–205°/10–12 mm. The distillate is a yellow liquid which soon solidifies to a light yellow solid. The side arm of the distilling flask should be of rather large bore (about 10 mm.) to prevent clogging by the amine which solidifies. The crude product weighs 220–235 g. and melts at 120–124°.

In order to obtain a pure product the amine is dissolved in about 700 cc. of boiling ethyl acetate under a reflux condenser. When the amine has dissolved the solution is rapidly cooled and stirred, whereupon the amine separates in almost white crystals. Further crops of crystals may be obtained on concentrating the solution and cooling. The last portions may be colored, but one

crystallization from ethyl acetate gives a nearly colorless product (Note 12). The total yield of pale yellow product which melts at 126° is 200–210 g. (82–85 per cent of the theoretical amount) (Note 13).

## 2. Notes

1. The air condenser used here was 65 cm. long and of 13 mm. bore and the vertical water condenser, 40 cm. in length. Cork stoppers were used and it was found desirable to protect their exposed surfaces by coating them with water glass, allowing these to dry, and then coating with lead foil. It is best to boil the mixture on a sand bath and to cover with asbestos that part of the flask not immersed in the sand.

2. Technical diphenylamine which has been vacuum distilled and collected over a 5° range (159–164°/4 mm.) is satisfactory.

3. The nitrobenzene should not contain any free acid. Should there be free acid present, it can be removed by shaking with solid potassium carbonate.

4. "Natur Kupfer C" is a good catalyst, but ordinary copper bronze may be used.

5. The time required for the completion of reaction varies with the rate of stirring. When the stirring is very vigorous most of the water comes over within twelve hours.

6. This heating should be done carefully, preferably on a sand bath, because of the danger of breaking the flask due to the caking of some undissolved potassium carbonate.

7. In general, about 8–10 l. of aqueous distillate is required, and practically all but about 25 cc. of the nitrobenzene is recovered. It is recommended that the removal of nitrobenzene by steam distillation be fairly complete in order to avoid a gummy residue.

8. Most of the iodine can be recovered as potassium iodide mixed with some potassium carbonate. A little cuprous iodide is also present.

9. The hydrogen chloride is introduced through a delivery tube at least 25 mm. in diameter and about 10 cm. under the

surface of the liquid. If the gas is introduced rapidly enough and the mixture occasionally stirred there is little trouble with clogging of the delivery tube.

10. The crude diphenylamine may be recovered by decomposing the hydrochloride with water and filtering the mixture.

11. A large amount of hydrogen chloride is evolved during the distillation and some provision must be made to keep it out of the room.

12. Because of the lesser solubility of triphenylamine in ethyl alcohol this solvent may be used advantageously in washing the crystals and in recrystallizing small amounts of the compound.

13. N-Phenyl carbazole may be made in an analogous manner by using carbazole in place of diphenylamine. If stirring and heating are both very vigorous, twelve hours suffice for the reaction. The yield of purified product is about 88 per cent and the compound melts at 88–89°. The crystals, when crushed, emit a strong violet light.

### 3. Methods of Preparation

This procedure is a modification of the method of Goldberg and Nimerovsky.[1] Triphenylamine has also been prepared by the treatment of aniline or diphenylamine with potassium and then bromobenzene [2] and by the action of sodium on diphenylamine and bromobenzene.[3]

[1] Goldberg and Nimerovsky, Ber. **40**, 2452 (1907).

[2] Merz and Weith, Ber. **6**, 1514 (1873).

[3] Heydrich, Ber. **18**, 2156 (1885).

# LATER REFERENCES TO PREPARATIONS IN PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been described during 1926. The numbers in parentheses following the name of a compound refer to the volume and page of Organic Syntheses).

**Acrolein** (6, 1):

By heating glycerol with anhydrous magnesium sulfate. EVANS and HASS, J. Am. Chem. Soc. **48**, 2703 (1926).

**Benzene sulfonyl chloride** (1, 21):

From sodium benzene sulfonate and chlorosulfonic acid. RODIONOV, Bull. soc. chim. (4) **39**, 305 (1926).

**Benzil** (1, 25):

By the oxidative catalytic dehydration of benzoin. ZETZSCHE and ZALA, Helvetica Chim. Acta **9**, 288 (1926).

**Benzilic acid** (1, 29):

By heating benzil in toluene with sodamide and treatment with water. KASIWAGI, Bull. Chem. Soc. Japan **1**, 66 (1926) [C. A. **20**, 2491 (1926)].

***n*-Butyl *n*-butyrate** (5, 23):

A by-product in the preparation of butyraldehyde by the dehydrogenation of butyl alcohol with a copper catalyst. LEGG and BOGIN, U. S. pat. 1,580,143 (1926) [C. A. **20**, 1813 (1926)].

**Ethyl Bromide** (1, 6):

From ethyl *p*-toluene sulfonate and potassium bromide. RODIONOV, Bull. soc. chim. (4) **39**, 305 (1926).

**Ethyl oxalate** (2, 22, and 5, 59):

(*a*) *To oxalic acid is added sufficient alcohol to remove* as the azeotropic mixture all of the water formed in the reaction and then the mixture is heated until the water is removed. CONTZEN-CROWET, Bull. soc. chim. Belg. **35**, 165 (1926).

(*b*) Essentially the method given in Organic Syntheses. WAHL, Bull. soc. chim. (4) **37**, 713 (1925).

**2-Furancarboxylic acid and 2-Furylcarbinol** (6, 44):

By heating furfural in toluene with sodamide. KASIWAGI, Bull. Chem. Soc. Japan **1**, 66 (1926) [C. A. **20**, 2491 (1926)].

**Furfural** (1, 49):

(*a*) From peanut hulls. DE BELSUNCE, Bull. mat. grasses **1926**, 1.

(*b*) By the oxidative catalytic dehydration of furfuralcohol. ZETZSCHE and ZALA, Helvetica Chim. Acta **9**, 288 (1926).

***d*-Glutamic acid** (5, 63):

(*a*) By the electrolysis of beet sugar residues. TAKAYAMA, Brit. pat. 233,196 (1924) [C. A. **20**, 675 (1926)].

(*b*) By the hydrolysis of the residues from alcoholic fermentation. IKEDA, U. S. pat. 1,582,472 (1926) [C. A. **20**, 1996 (1926)].

(*c*) From acrolein through $\gamma$-aldehydobutyric acid. KEIMATSU and SUGASAWA, J. Pharm. Soc. Japan **531**, 369 (1925) [C. A. **20**, 2824 (1926)].

**Mesityl oxide** (1, 53):

(*a*) From acetone and sulfuric acid. YLLNER, Svensk. Kem. Tids. **37**, 227 (1925) [C. A. **20**, 739 (1926)].

(*b*) From acetone and phosphorus oxychloride. GASOPOULOS, Ber. **59**, 2188 (1926).

**Myristic acid** (6, 66):

An improvement over the general procedure given in organic syntheses is described. VERKADE and COOPS, Rec. trav. chim. **46**, 528. (1927).

**Phenylacetic acid** (**2**, 63):

By the action of carbon dioxide on benzyl magnesium bromide. Ivanov, Bull. soc. chim. (4) **37**, 287 (1925).

**Phenylacetylene** (**2**, 67):

By the action of sodamide on styrene dibromide and on $\alpha$-bromostyrene. Bourguel, Ann. chim. (10) **3**, 225, 228 (1925).

**Pinacol hydrate** (**5**, 87):

A general study of the reduction of acetone to pinacol. Calvert, India Rubber Rev. **26**, No. 9, 48 (1926).

**Quinone** (**2**, 85):

By the oxidation of hydroquinone in 60 per cent acetic acid with chromic acid. Craven and Duncan, J. Chem. Soc. **127**, 1489 (1925).

**1,2,3-Tribromopropane** (**5**, 99):

By the bromination of 1,2-dibromopropane in the presence of iron. Tapley and Giesy, J. Am. Pharm. Assoc. **15**, 173 (1926).

# ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of a compound, refer to a number and page of "Organic Syntheses.")

Cyclohexylcarbinol (**6**, 22). In the preparation of cyclohexylcarbinol as described in Vol. **6**, 22, a high-boiling by-product, the cyclohexylcarbinol acetal of formaldehyde, is sometimes obtained. The by-product becomes the main product if the steam distillation of the reaction mixture is omitted. The by-product can usually be avoided if twice the calculated amount to decompose the Grignard reagent of 10 per cent sulfuric acid is added to the reaction mixture before steam distillation is carried out. The acetal which may be present is thus hydrolyzed.

If acetal has been isolated, it may best be hydrolyzed by boiling with an equivalent weight of ethyl alcohol and concentrated hydrochloric acid (2 cc. for each 50 cc. of alcohol used) for four or five hours, then distillation of the ethyl alcohol, and treatment with water.

Ketene (**4**, 39). It has been found that the formation of acetanilide from ketene and aniline takes place more satisfactorily if the ketene is passed directly into excess aniline without any dry ether present. The excess aniline may then be removed by vacuum distillation until the temperature of the vapors is 10–15° higher than the boiling point of aniline. An alternative plan is to remove excess aniline by dilute hydrochloric acid, to filter the acetanilide and to wash with water.

Phenylacetylene (**2**, 67). It is stated in the directions that the distilling flask is heated until a temperature of 200° is reached and at that temperature the potassium hydroxide which is used is molten. The potassium hydroxide usually available contains sufficient moisture so that it will liquefy at 200°. If pure dry potassium hydroxide is used, it is necessary to add a little water so that the fusion point will be lowered to the point indicated.

Another contributor has offered the suggestion that just as good yields can be obtained if the eutectic of sodium hydroxide and potassium hydroxide is employed, under which conditions the alkali is molten at 200° and the reaction takes place very readily.

# AUTHOR INDEX

(This index comprises names from all volumes of this series. The numbers after each name refer to a volume and page in "Organic Syntheses.")

# SUBJECT INDEX

*(This Index Comprises Material from all Volumes of this Series)*

(Names of compounds in small capital letters indicate substances for which directions are given, the numbers in bold face type refer to volumes of Organic Syntheses, numbers in italics refer to pages in those volumes on which preparative directions are given, and numbers in Arabic refer to pages on which the compounds or subjects are mentioned in connection with other preparations. For example: ACETOACETIC ESTER, **4**, 45; **6**, *36* indicates that acetoacetic ester is mentioned in volume 4 on page 45 and that directions for its preparation are given in detail in volume 6 on page 36; Acetophenone, **2**, 1 indicates that this substance is mentioned in volume 2 on page 1 but that no directions for its preparation are given in this series).

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# ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS



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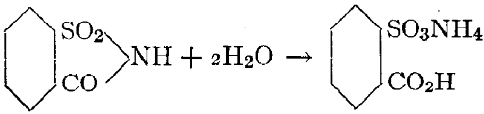
# ORGANIC SYNTHESES

## I

### ACID AMMONIUM *o*-SULFOBENZOATE



Submitted by H. T. Clarke and E. E. Dreger.
Checked by Henry Gilman and J. E. Kirby.

#### 1. Procedure

In a 12-l. flask fitted with a stirrer and reflux condenser are placed 188 g. (1 mole) of *o*-sulfobenzoic imide ("saccharin insoluble"), 565 cc. of distilled water and 188 g. of concentrated hydrochloric acid (sp. gr. 1.19). The mixture is boiled over a free flame with continual stirring (Note 1) until all the solid is in solution; this requires two and one-half to three hours. A second quantity of 188 g. of *o*-sulfobenzoic imide is then added, and the mixture again heated with stirring until a clear solution results, which requires one and one-half to two hours. Heating is then continued for one hour longer, whereupon the solution is poured into a crock and allowed to cool. The crystals which separate are collected on a suction funnel, washed as free from hydrochloric acid as possible (Note 2) with ice-cold distilled water, and dried. The mother liquor and washings are concentrated on a steam bath under reduced pressure until the separation of crystals causes bumping, when the solution is again allowed to crystallize. This procedure is repeated, the final mother liquor being evaporated nearly to dryness. The

main product, together with that from the mother liquors, weighs 410–427 g. (91–95 per cent of the theoretical amount) and is sufficiently pure for conversion into *o*-sulfobenzoic anhydride. In order to obtain a purer product the material may be recrystallized from an equal weight of distilled water; the yield on recrystallizing is about 90 per cent.

## 2. Notes

1. The mixture tends to foam somewhat during the first few minutes of boiling.

2. If much hydrochloric acid is allowed to remain with the crystals, drying is extremely difficult.

## 3. Methods of Preparation

Acid ammonium *o*-sulfobenzoate has been prepared by the hydrolysis of saccharin with concentrated hydrochloric acid.[1] The above method is a modification of that of White and Acree.[2]

[1] Fahlberg and Barge, Ber. **22**, 755 (1889); Remsen and Linn, Am. Chem. J. **11** 74 (1889).

[2] White and Acree, J. Am. Chem. Soc. **41**, 1197 (1919).

## *dl*-ALANINE

$$CH_3CHO + NH_4Cl + NaCN \rightarrow CH_3CHNH_2CN + NaCl + H_2O$$

$$CH_3CHNH_2CN + 2H_2O + 2HCl \rightarrow CH_3CH(NH_3Cl)CO_2H + NH_4Cl$$

$$2CH_3CH(NH_3Cl)CO_2H + Pb(OH)_2 \rightarrow 2CH_3CHNH_2CO_2H + PbCl_2 + 2H_2O$$

Submitted by E. C. KENDALL and B. F. MCKENZIE.
Checked by C. S. MARVEL and W. W. MOYER.

### 1. *Procedure*

ONE hundred and thirty-two grams (3 moles) of freshly distilled acetaldehyde (Note 1) is added to 100 cc. of ether in a 2-l. bottle and cooled to 5° in an ice bath (Note 2). One hundred and eighty grams (3.4 moles) of ammonium chloride dissolved in 550 cc. of water is then added, followed by an ice-cold solution of 150 g. (3 moles) of sodium cyanide in 400 cc. of water. The sodium cyanide must be added slowly and with frequent cooling to prevent loss of acetaldehyde by volatilization.

After the sodium cyanide solution is added, the bottle is stoppered securely, placed in a mechanical shaker, and shaken for four hours at room temperature. At the end of this time the solution is transferred to a 3-l. distilling flask and 600 cc. of concentrated hydrochloric acid (sp. gr. 1.19) is added (Note 3).

The solution in the flask is distilled over a free flame until separation of salt prevents further heating. It is then transferred to a large evaporating dish, placed on a steam-bath and evaporated to dryness (Note 4).

The residue remaining in the dish after evaporation is stirred

thoroughly with 800 cc. of 95 per cent alcohol. After filtration the alcohol is distilled on a steam bath and the last traces are removed under vacuum. While still warm the residue is dissolved in 500 cc. of 95 per cent alcohol containing 2 per cent of hydrochloric acid, and cooled. Two hundred cubic centimeters of ether is added, and the solution is filtered. This treatment should remove all but the last traces of sodium chloride and ammonium chloride. The alcohol and ether are removed by distillation and the last of the free hydrochloric acid is removed by distillation under diminished pressure.

The alanine hydrochloride remaining in the flask is dissolved in 1500 cc. of water, and transferred to a metal pail of about 2-l. capacity. Two hundred and twenty grams of yellow lead oxide is added and the mixture is boiled gently for one hour. During the boiling small amounts of water are added at intervals in order to maintain the original volume (Note 5). Upon cooling, the lead chloride crystallizes; it is filtered off and the solution is again boiled one hour with 100 g. of lead oxide. Twenty grams of freshly precipitated lead hydroxide is added slowly and the boiling is continued for ten minutes. Following this the solution is again cooled and filtered (Note 6). The chloride content should now be not more than 50–75 cc. of a normal solution (Note 7).

The solution is again brought to a boil and a calculated amount of silver oxide (Note 7) is added to remove the last of the chlorides. The silver chloride is filtered off and the lead is precipitated with hydrogen sulfide. A light straw-colored solution remains.

The solution is evaporated by boiling to a volume of about 400 cc., and 600 cc. of 95 per cent alcohol is added. When thoroughly cooled, 100–120 g. of alanine is filtered off. This is washed with 200 cc. of alcohol and a pure white product is obtained.

A further crop of 40–50 g. may be obtained by removing the alcohol and water until a volume of about 100 cc. remains, and then adding 250 cc. of alcohol and cooling to 0°. The total yield is 140–160 g. (52–60 per cent of the theoretical amount).

Alanine so prepared is sufficiently pure for most purposes. It may be recrystallized by dissolving in the least amount of water and adding two volumes of alcohol.

## 2. Notes

1. Acetaldehyde may be conveniently prepared by distilling from paraldehyde in the presence of a trace of sulfuric acid; an efficient fractionating column should be used.

2. A one-half-gallon ginger-ale bottle is convenient for this purpose. The necks of these bottles are small and will hold a wire securely.

3. Caution must be observed during the addition of the hydrochloric acid as considerable hydrogen cyanide is evolved. During the first part of the subsequent distillation it is necessary to prevent fumes from escaping from the receiver into the room.

4. During the evaporation a layer of crystals forms on the surface and must be continually broken. A blast of air blowing over the surface agitates the liquid sufficiently and allows free evaporation.

5. The volume of the solution must be kept large during the treatment with lead oxide as lead chloride will not crystallize from concentrated alanine solutions.

6. If the solution at this point still contains ammonium salts another treatment with 100 g. of lead oxide is necessary.

7. An aliquot portion of the solution is titrated with silver nitrate by the Volhard method. The result of this titration is used in calculating the amount of silver oxide which must be added.

## 3. Methods of Preparation

*dl*-Alanine has been prepared by heating ethyl $\alpha$-chloropropionate with concentrated aqueous ammonia at 100°;[1] by warming $\alpha$-bromopropionic acid with alcoholic ammonia;[2] by

[1] H. Kolbe, Ann. **113**, 221 (1860).
[2] Kekulé, Ann. **130**, 18 (1864).

reducing $\alpha$-oximinopropionic acid with zinc in hydrochloric acid;[3] by reduction of *dl*-serine with hydriodic acid and red phosphorus;[4] by heating cysteine hydrochloride to 140–150°;[5] and by heating hydropyruvinureide with aqueous barium hydroxide.[6]

Strecker[7] first synthesized alanine by the action of hydrocyanic acid on aldehyde ammonia. The present procedure is based on Zelinsky's modification of the Strecker synthesis.[8]

[3] Gutknecht, Ber. **13**, 1118 (1880).
[4] Fischer and Leuchs, Chem. Zentr. **1902 I**, 762.
[5] Mörner, Z. physiol. Chem. **42**, 360 (1909).
[6] Gabriel, Ann. **348**, 70 (1906).
[7] Strecker, Ann. **75**, 29 (1850).
[8] Zelinsky, Stadnikow, Ber. **41**, 2061 (1908).

# AMMONIUM SALT OF AURIN TRICARBOXYLIC ACID

$$3\ o\text{-}HOC_6H_4CO_2H + CH_2O + 4NaNO_2 + 4H_2SO_4 \rightarrow$$
$$O{=}C_6H_3(CO_2H){=}C(C_6H_3(OH)CO_2H)_2 + 4NO + 4NaHSO_4 + 5H_2O$$

Submitted by G. B. HEISIG and W. M. LAUER.
Checked by H. T. CLARKE and ROSS PHILLIPS.

## 1. Procedure

To 70 cc. of concentrated sulfuric acid (Note 1) in a 1-l. short-neck flask fitted with a mechanical stirrer and immersed in an ice-water bath is added, with vigorous stirring, 10 g. (0.145 moles) of solid sodium nitrite in small portions. The addition is made at such a rate that only a very small amount of nitrogen oxide is evolved. When solution is complete, 20 g. (0.145 moles) of salicylic acid is added in small portions with stirring; about fifteen minutes is required. The mixture is stirred at 20° until all the solid is in solution (Note 2). The mixture should then be light red to brown in color, very viscous, and quite homogeneous. It is surrounded by an ice-salt bath and when the temperature reaches 0°, 5 cc. (0.065 mole) of a 35–40 per cent solution of formaldehyde (formalin) *is slowly* added with extremely vigorous stirring, at such a rate that the temperature does not rise above 5° (Note 3). The reaction is complete a few minutes after all the formaldehyde has been added. About 100 g. of finely crushed ice is then added, followed by 500 cc. of ice-water; *the stirring should be vigorous* during the addition (Note 4). The contents of the flask are stirred until the aurin tricarboxylic acid has disintegrated into small pieces. The solid is washed several times by decantation,

using cold water, and finally filtered with suction. It is then dissolved in dilute ammonia (1 volume of concentrated ammonia with 2 volumes of water) while it is still on the filter paper in the suction funnel (Note 5). The filtrate is evaporated to dryness on a steam bath. The resulting glassy, light yellowish-brown ammonium salt, which weighs 19–22 g. (83–96 per cent of the theoretical amount) is sufficiently pure (Note 6) for use as a test for aluminium.

## 2. Notes

1. The reaction may be carried out somewhat less satisfactorily with the use of 55 cc. of sulfuric acid.

2. If solution is not complete, unchanged salicylic acid will be present in the final product.

3. If the stirring is quite violent, the temperature may be allowed to rise somewhat higher, say to 15–20°, but if the temperature is allowed to rise with only moderate stirring, the yield is lowered owing to the formation of tars.

4. Foaming may occur during the addition of the water but this can be controlled by adding a few drops of ether.

5. The purification of the crude aurin tricarboxylic acid by extracting with hot water[1] is undesirable, for the hot water causes the acid to soften, and results in the formation of large viscous semi-liquid masses which cannot be filtered readily.

6. The method suggested by Caro[2] for the purification of aurin tricarboxylic acid seems to be unnecessary when the dye is to be used as a test for aluminium. In this method the crude product is dissolved in sodium hydroxide, sodium bisulphite is added until the solution is decolorized, and the addition compound of the free acid is precipitated by adding hydrochloric acid.

## 3. Methods of Preparation

The preparation of aurin tricarboxylic acid was first described in a patent[3] granted to Geigy, in which the foregoing method is

[1] Hammett and Sottery, J. Am. Chem. Soc. **47**, 142 (1925).
[2] Caro, Ber. **25**, 939 (1892).
[3] Geigy, Ger. Pat. 49970, Frdl. **2**, 50 (1891).

embodied in one of the examples; another method, involving the action of sodium nitrite upon a warm solution of salicylic acid in a mixture of methyl alcohol and sulfuric acid, is also described in the same patent. It has also been prepared [4] by the action of sulfuric acid and nitrite upon a mixture of salicylic acid and 3.3′-dicarboxy–4.4′-dihydroxydiphenylmethane ("methylene disalicylic acid"), which is formed from salicylic acid with formaldehyde in presence of hydrochloric acid.

Aurin tricarboxylic acid is of interest as a reagent for detecting aluminium.[5]

[4] Caro, Ber. **25**, 939 (1892).

[5] Hammett and Sottery, J. Am. Chem. Soc. **47**, 142 (1925).

IV

## ANISOLE

$$C_6H_5OH + NaOH \rightarrow C_6H_5ONa + H_2O$$

$$2C_6H_5ONa + (CH_3)_2SO_4 \rightarrow 2C_6H_5OCH_3 + Na_2SO_4$$

Submitted by G. S. HIERS and F. D. HAGER.
Checked by HENRY GILMAN, S. A. HARRIS, and G. WRIGHT.

### 1. Procedure

IN a 5-l. two-neck round-bottom flask fitted with an efficient stirrer, separatory funnel, and reflux condenser is placed a mixture of 235 g. (2.5 moles) of phenol and 100 g. (2.5 moles) of sodium hydroxide (Note 1) in 1 l. of water. The mixture is cooled, with stirring, in an ice-salt bath to below 10°. There is then added through the separatory funnel 315 g. (2.5 moles) of dimethyl sulfate (Note 2). This addition requires about one hour and the cooling bath is not removed until the addition is complete. The mixture is then heated on a water bath for half an hour. At the end of this time there is added through the separatory funnel a mixture of 235 g. (2.5 moles) of phenol and 100 g. (2.5 moles) of sodium hydroxide in 1 l. of water. This addition requires about fifteen minutes. The mixture is then refluxed vigorously over a free flame for fifteen hours (Note 3).

The mixture is cooled and the anisole layer is separated. The aqueous portion is extracted with about 200 cc. of benzene (Note 4). The combined anisole-benzene portion is washed once with water, dried over calcium chloride and distilled from a modified Claisen flask (Org. Syn. 1, 40). The portion boiling at 100–153° is refractionated. The main fraction distills at 153–154°/748 mm. The yield is 388–405 g. (72–75 per cent of the theoretical amount) (Notes 5 and 6).

## 2. Notes

1. The sodium hydroxide was a high quality technical grade.

2. Dimethyl sulfate is toxic, but with due care to avoid spattering of the liquid and inhaling of the vapor the operation may be carried out without the use of a hood. A good technical grade of dimethyl sulfate was used.

3. When the period of refluxing is shorter, the yield is materially decreased. The first methyl group reacts easily but the second only with considerable difficulty. A longer period of refluxing does not give much larger yields. As the sodium sulfate concentration increases, the dimethyl sulfate hydrolyzes less readily.

4. A separate fractional distillation of this benzene extract yields 9–18 g. of anisole. The major part of the anisole contained in the aqueous layer may be recovered by steam distillation instead of a benzene extraction. Neither method of recovery is wholly satisfactory.

5. When only one-half the amount of phenol is used, the yield is 85–92 per cent but with fairly inexpensive phenol it is more profitable to operate in such a manner that both methyl groups of the dimethyl sulfate are used.

6. Other methyl ethers may be prepared by a similar procedure. $\beta$-Naphthyl methyl ether is obtained in a 65–73 per cent yield by adding the dimethyl sulfate over a period of thirty minutes to equivalent quantities of $\beta$-naphthol and sodium hydroxide kept cool by an ice-water bath, then heating for one hour at 75–78°, and, finally, crystallizing from benzene to obtain the pure methyl ether which melts at 71°.

## 3. Methods of Preparation

Anisole has been prepared by a variety of other methods, the most important being: from sodium or potassium phenolate and methyl iodide;[1] from sodium phenolate and methyl chloride;[2]

[1] Cahours, Ann. 78, 225 (1851); Segaller, J. Chem. Soc. **105**, 112 (1914).
[2] Vincent, Bull. soc. chim. (2) **40**, 106 (1883).

from potassium phenolate and sodium methyl sulfonate;[3] from benzene diazonium nitrate and methyl alcohol;[4] sodium benzene sulfonate and sodium methylate;[5] phenol and methyl alcohol in the presence of thorium oxide;[6] from phenol, methyl alcohol and $\beta$-naphthalene sulfonic acid[7] or potassium hydrogen sulfate;[8] and by the methylation of phenol with dimethyl sulfate or methyl ethyl sulfate.[9]

[3] Nollau and Daniels, J. Am. Chem. Soc. **36** 1890 (1914).
[4] Beeson, Amer. Chem. J. **16**, 235 (1894).
[5] Moureu, Bull. soc. chim. (3) **19**, 399 (1898).
[6] Sabatier and Mailhe, Compt. rend. **151**, 359 (1910).
[7] Krafft and Roos, Ger. pat. 76, 574, Frdl. IV, 17.
[8] Actiengesellschaft für anilinfabrikation in Berlin, Ger. pat. 23, 775, Frdl. I, 43.
[9] Thayer, J. Am. Chem. Soc. **46**, 1046 (1924).

# V

## BENZOYL PIPERIDINE

$$C_5H_5N + 6[H] \rightarrow C_5H_{11}N$$

$$C_5H_{11}N + C_6H_5COCl + NaOH \rightarrow C_5H_{10}NCOC_6H_5 + NaCl + H_2O$$

Submitted by C. S. Marvel and W. A. Lazier.
Checked by J. B. Conant, J. S. Andrews, and C. O. Tongburg.

### 1. Procedure

In a 5-l. two-neck round-bottom flask, fitted with an efficient reflux condenser (Note 1), is placed a mixture of 130 g. (1.64 moles) of dry pyridine (Note 2) and 3 l. of absolute alcohol. During the course of forty to fifty minutes 450 g. (19.6 moles) of sodium is added gradually. The sodium is added in as large pieces as can be inserted through the second opening in the flask. One and one-half liters of absolute alcohol is now added and the mixture heated over an oil bath for two to three hours until the sodium disappears. It is desirable not to allow the reaction mixture to cool (Note 3) at this point but to separate the piperidine immediately. The condenser is set for distillation and a separatory funnel is inserted through the stopper in the second opening of the flask. The alcohol is then distilled using an oil bath (Note 4). The addition of a piece of zinc facilitates an even distillation. During this procedure, water to the amount of 1700–1800 cc. is added to the reaction mixture through the separatory funnel, slowly at first and later as rapidly as possible. At the beginning, this addition must be very cautious as the heat evolved causes a very rapid distillation of alcohol. After about 200 cc. of water has been added, the mixture begins to solidify and remains semi-solid until most of the water has been added.

The distillation is continued until practically all the alcohol has distilled (three to four hours). At the end of this time there remains in the distilling flask about 1500 cc. of residue, which is discarded. The distillate is about 5 l. in volume. To this is added 200 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and the mixture is then returned to the distilling flask. The alcohol is removed by distillation on a steam bath until the residual volume in the flask amounts to about 600–800 cc.; this requires two to three hours. The residue is then transferred to a 2-l. round bottom flask fitted with a mechanical stirrer and separatory funnel. The mixture is treated with stirring with a solution of 186 g. of technical sodium hydroxide or 170 g. (4.25 moles) of c. p. sodium hydroxide in about 300 cc. of water. With continuous stirring 235 g. (1.67 moles) of benzoyl chloride is now added during the course of an hour, keeping the temperature down by cooling with running water. After the addition, the reaction mixture is cooled, the amide separated (Note 5), washed with a little water (Note 6) and distilled (Note 7) under reduced pressure. The product boils at 180–184°/20 mm., 191–194°/27 mm., 240–244°/130 mm., and weighs 240–250 g. (77–81 per cent of the theoretical amount).

Benzoyl piperidine thus obtained is a straw-colored viscous liquid. Upon long standing or seeding with crystalline benzoyl piperidine, the compound crystallizes in long, colorless needles which melt at 44°. The literature reports 48° as the melting point of the pure material.

Using 180 g. of pyridine in place of the 130 g. suggested, and a corresponding increase in the other chemicals except the sodium and alcohol, a yield of 300–326 g. of benzoyl piperidine is obtained. This is a smaller percentage yield (70–75 per cent of the theoretical amount) but the actual yield more than repays for the excess of pyridine used (see also Note 8).

## 2. Notes

1. A reflux condenser 80 cm long with inner tube 2 cm. in diameter is recommended. If a smaller condenser is employed,

the reaction cannot be run as rapidly as is desirable to give the best results. If the reaction is not run rapidly sodium ethylate separates in the flask.

2. Unless the purity of the pyridine is known, it should be dried with solid sodium hydroxide and distilled before use. For this work a fraction boiling at 112–117° was used.

3. If the alcohol solution is allowed to cool before the addition of the water, it solidifies and is remelted only with difficulty. If it is desired to suspend the process, the water should be added first and then the solution will not solidify.

4. In distilling the piperidine from the strong alkaline solution, the flask must be suspended in the oil bath. Direct heating raises the temperature of flask to such a point that the alkali rapidly eats through it.

5. A troublesome emulsion sometimes results after benzoylation. This may be broken up usually by the addition of more strong sodium hydroxide solution. In case an emulsion is formed which cannot be broken it is possible to extract the product with benzene.

6. Any sodium hydroxide carried into the distilling flask causes decomposition of the benzoyl piperidine during distillation and consequently a considerably lower yield results. For this reason it is well to wash the product carefully in the separatory funnel with a little water after the alkaline solution has been drawn off.

7. Benzoyl piperidine is much given to superheating, making distillation difficult.

8. If piperidine is available, benzoyl piperidine for use in the preparation of pentamethylene bromide (p. 70) may be prepared by direct benzoylation. A mixture of 105 g. of sodium hydroxide (2.6 moles), 170 g. of piperidine (2.0 moles) (b. p. 104–108°) and 800 cc. of water are treated with 280 g. (2 moles) of benzoyl chloride using the apparatus and procedure described above; the temperature is kept at 35–40°. The oily product is separated after dilution with 250 cc. of benzene if necessary (Note 5), dried with a small quantity of potassium carbonate and distilled. The portion boiling at 172–174°/12 mm. weighs 330–345 g. (87–91 per cent of the theoretical amount). The first few

cubic centimeters of the distillate may be colored by a reddish impurity in which case a fore-run is collected separately.

## 3. Methods of Preparation

Benzoyl piperidine has been prepared only by the action of benzoyl chloride on piperidine in the presence of alkalies.[1]

[1] Cahours, Ann. chim. phys. (3) **38**, 87 (1853); Schotten, Ber. **17**, 2545 (1884); **21**, 2238 (1888).

# *p*-BROMOPHENACYL BROMIDE

$$BrC_6H_4COCH_3 + Br_2 \rightarrow BrC_6H_4COCH_2Br + HBr$$

Submitted by W. D. LANGLEY.
Checked by H. T. CLARKE and P. W. BOUTWELL.

## 1. Procedure

IN a 500-cc. flask are placed 50 g. (0.25 mole) of *p*-bromoacetophenone (Org. Syn. **5**, 17) and 100 cc. of glacial acetic acid. To the resulting solution is very slowly added 40 g. (0.25 mole) of bromine, keeping the temperature below 20°. The mixture is vigorously shaken by hand during the addition. *p*-Bromophenacyl bromide begins to separate as needles when about one-half of the bromine has been added. The addition requires about thirty minutes.

When all the bromine has been added, the flask is cooled in ice-water and the product filtered with suction. The crude crystals are washed with 50 per cent ethyl alcohol until colorless (about 100 cc. is required). The material so obtained, when air-dried, melts at 106–108° and weighs 55–60 g. It is recrystallized from 400 cc. of 95 per cent ethyl alcohol, from which it separates as colorless needles melting at 108–109°. The yield (Note 1) is 48–50 g. (69–72 per cent of the theoretical amount).

## 2. Notes

1. A further quantity of less pure material may be obtained from the mother liquor from the recrystallization. If the acetic acid mother liquor is treated with water until turbid and then chilled, 4–5 g. of yellow crystals may be obtained. The material recovered from both liquors (6–8 g. in all) cannot be obtained

in a perfectly colorless condition but the melting point is correct after recrystallization from alcohol.

2. Judefind and Reid[1] have shown that many acids may be identified by conversion into their *p*-bromophenacyl esters by the action of *p*-bromophenacyl bromide on the sodium salts.

### 3. *Methods of Preparation*

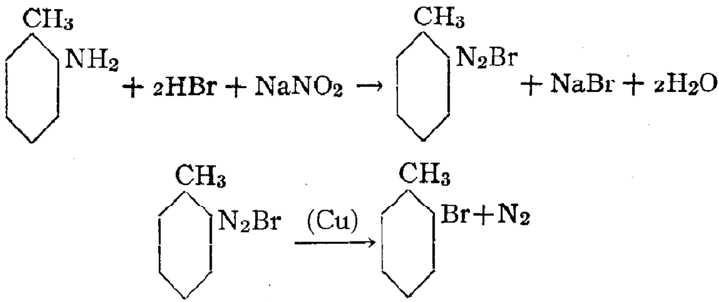
*p*-Bromophenacyl bromide has been prepared by the interaction of bromobenzene and bromoacetyl chloride in the presence of aluminum chloride[2] and by the bromination of *p*-bromoacetophenone.[1, 3]

[1] Judefind and Reid, J. Am. Chem. Soc. **42**, 1045 (1920).

[2] Collet, Compt. rend. **125**, 717 (1897).

[3] Collet, Bull. soc. chim. (3) **21**, 67 (1899).

## *o*-BROMOTOLUENE



Submitted by L. A. Bigelow.
Checked by C. S. Marvel and S. V. Puntambeker.

### 1. Procedure

A solution of 162 g. (1.5 moles) of commercial *o*-toluidine in 880 cc. (6 moles) of 40 per cent commercial hydrobromic acid (Note 1) in a 3-l. flask is cooled to 10° and diazotized with 116 g. (1.7 moles) of coarsely powdered commercial sodium nitrite, added about 10 g. at a time. After each addition the flask is stoppered and shaken until all the red fumes are absorbed. The temperature must be kept below 10°. When diazotization is complete, 5 g. of copper powder (Note 2) is added, the flask is attached to a reflux condenser and heated very cautiously. As soon as the first sign of reaction is observed, the flask is cooled with ice. Nitrogen is evolved vigorously. When the reaction subsides, the mixture is heated half an hour on the steam bath. Then 1 l. of water is added and the mixture is distilled with steam until about 1.5 l. has passed over. The distillate is made alkaline with about 10 g. of powdered sodium hydroxide and the red bottom layer of crude *o*-bromotoluene separated (Note 3).

This weighs about 140 g. It is washed with concentrated sulfuric acid, which removes almost all the color, and then twice with water. It is dried over a little calcium chloride, filtered and distilled twice from a modified Claisen flask (Org. Syn. 1, 40). The yield of pure product boiling at 178–181° is 110–120 g. (42–47 per cent of the theoretical amount).

## 2. Notes

1. If 48 per cent (constant boiling) hydrobromic acid is used the diazotization is very difficult to control. The reaction becomes very vigorous and forces out the stopper.

2. Either reduced copper or fine copper filings may be used.

3. This gives as good results as when the *o*-bromotoluene is extracted from the alkaline mixture with ether.

## 3. Methods of Preparation

*o*-Bromotoluene has been obtained by the bromination of toluene;[1] by the bromination of potassium *p*-toluene sulfonate and subsequent hydrolysis;[2] and by diazotization of *o*-toluidine under different conditions.[3]

[1] Jannasch and Hübner, Ann. **170**, 117 (1873).

[2] Miller, J. Chem. Soc. **61**, 1027 (1892).

[3] Wroblevsky, Ann. **168**, 171 (1873); Koerner, Gazz. chim. ital. **4**, 305 (1874); Jackson, Am. Chem. J. **1**, 100 (1879); Feitler, Z. physik. Chem. **4**, 72 (1889).

VIII

# *n*-BUTYL CARBAMATE

$$NH_2CONH_2 \rightarrow NH_3 + HNCO$$

$$HNCO + C_4H_9OH \rightarrow NH_2CO_2C_4H_9$$

Submitted by TENNEY L. DAVIS and STANLEY C. LANE.
Checked by H. T. CLARKE and L. G. S. BROOKER.

## 1. Procedure

IN a 2-l. round-bottom flask fitted with a reflux condenser is placed 1200 cc. (970 g., 13.1 moles) of *n*-butyl alcohol. This is warmed and 180 g. (3 moles) of urea is added to the warm liquid in small portions, with shaking, while the temperature rises, care must be taken that the urea goes into solution without melting and does not form a layer of molten urea beneath the solution (Note 1). The last portions of the urea are finally dissolved by boiling the liquid. The solution is then refluxed for thirty hours (Note 2), during which time ammonia escapes from the top of the condenser (Note 3). The reflux condenser is then removed and the liquid is distilled through an efficient column until the temperature of the liquid reaches 150°. The distillate consists of butyl alcohol containing ammonia and may be used directly in another run. The material which remains in the flask solidifies on cooling. It is boiled with 1 l. of ligroin (b. p. 60–90°) (Note 4), filtered, and the undissolved solid again boiled with two 100-cc. portions of ligroin, filtered and finally washed on the filter with 100 cc. more of warm ligroin. The white gritty material which remains undissolved is practically pure cyanuric acid (Note 5). The yield of cyanuric acid is 12–18 g. (9–14 per cent of the theoretical amount).

The combined ligroin filtrates and washings are distilled under atmospheric pressure, using a column, until the temperature of the liquid reaches 150°. The residue is then distilled under reduced pressure and the fraction boiling at 108–109°/14 mm. (Note 6) is collected. The product is pure and melts at 53–54°. The yield is 263–266 g. (75–76 per cent of the theoretical amount.)

## 2. Notes

1. If molten urea settles to the bottom near the source of heat, it will cause the liquid to bump and will decompose to produce cyanuric acid to the detriment of the yield of butyl carbamate.

2. If thirty hours of continuous heating is impracticable, care must be taken, on resuming the heating, that the urea goes into solution without melting.

3. A small amount of ammonium carbamate collects in the condenser during the reaction and may cause clogging. This should be removed from time to time by pushing it down by means of a glass tube which fits snugly into the condenser. The gases evolved when the solid falls into the hot liquid are carried off through the tube.

4. "Aviation" gasoline (86° Baumé) may also be employed if it is first distilled and the fraction boiling above 120° rejected.

5. The extraction with ligroin may be completed satisfactorily by means of the apparatus described in Org. Syn. **2**, 48 (1922). Butyl allophanate is not soluble in ligroin and, if present, would remain with the cyanuric acid. However, when the material which is insoluble in ligroin is washed with hot acetone the washings yield no appreciable residue on evaporation. This is evidence that butyl allophanate and urea are not present in the cyanuric acid.

6. *n*-Butyl carbamate boils under atmospheric pressure at 203–204° with some decomposition. The products of the decomposition are butyl alcohol and cyanuric acid.

### 3. Methods of Preparation

No reference to the preparation of *n*-butyl carbamate is to be found in the literature. The above process is adapted from that of Cahours,[1] who prepared *n*-propyl carbamate by heating propyl alcohol with urea. *n*-Butyl carbamate has also been prepared by one of the editors by the action of *n*-butyl chloroformate upon ammonia.

[1] Cahours, Compt. rend. **76**, 1387 (1873).

# *n*-BUTYL *p*-TOLUENESULFONATE

$$p\text{-}CH_3C_6H_4SO_2Cl + nC_4H_9OH + NaOH \rightarrow p\text{-}CH_3C_6H_4SO_2OC_4H_9 + NaCl + H_2O$$

Submitted by A. T. Roos, Henry Gilman, and N. J. Beaber.
Checked by H. T. Clarke and G. S. Babcock.

## 1. Procedure

In a 2-l., three-neck flask, fitted with a mechanical stirrer, a thermometer, and a 250-cc. separatory funnel, are placed 148 g. (2 moles) of *n*-butyl alcohol and 210 g. (1.1 moles) of pure *p*-toluenesulfochloride (Note 1). From the separatory funnel 320 cc. (1.6 moles) of 5 N sodium hydroxide is run in at a rate that does not cause the temperature of the reaction mixture to exceed 15° (Note 2); the addition requires three to four hours.

Another portion of 210 g. (1.1 moles) of *p*-toluenesulfochloride is added and then 320 cc. of 5 N sodium hydroxide solution is slowly introduced, again keeping the temperature below 15°. Stirring is continued for four hours longer, and the oily layer is separated from the water layer and any unchanged *p*-toluenesulfochloride. Enough petroleum ether (b. p. 60–70°) or benzene is added to the oil to cause it to float on water, the solution is washed thoroughly with 50 cc. of 10 per cent sodium hydroxide, and dried by standing overnight over 20 g. of anhydrous potassium carbonate. The solution is filtered, and the solvent is distilled. This is conveniently accomplished by adding the solution from a separatory funnel to a 500-cc. Claisen flask heated on a steam bath. The oily ester is then distilled in a vacuum (Note 3) and, after a forerun that comes over up to 170°/10 mm., the pure ester distils at 170–171°/10 mm. The yield is 250–270 g. (50–54 per cent of the theoretical amount).

## 2. Notes

1. Technical $p$-toluenesulfochloride is dissolved in benzene, washed with 5 per cent sodium hydroxide, dried by shaking with a small amount of potassium carbonate, and then distilled in a vacuum. If the vacuum distillation must be interrupted, it is recommended that the liquid be allowed to cool before breaking the vacuum; otherwise, when distillation is resumed later, considerable decomposition takes place.

2. The cooling may be effected conveniently by immersing the flask in a water bath containing a small amount of ice, or by cold running water. If the bath is cooled to 0°, the time required for the completion of the reaction is appreciably longer.

3. It is best to distil the ester under a very high vacuum. Appreciable decomposition takes place even at 10-mm. pressure, and the distilled ester becomes quite dark after standing a week. To avoid superheating and consequent decomposition, it is recommended that the ester be distilled in small lots (from 250-cc. Claisen flasks when large runs are made). A sample of 100 g. distilled at 132–133°/3 mm. remained water-white after standing for two months.

4. Methyl $p$-toluenesulfonate may be prepared in a somewhat similar manner with good yields. One kilo of methyl alcohol (90–95 per cent) is placed in a round-bottom flask, placed in an ice-salt bath. One kilo of powdered pure $p$-toluenesulfochloride (crude material may be used but the yield of product drops to about 75 per cent) is added with mechanical stirring. From a separatory funnel 840 g. of 25 per cent sodium hydroxide solution is added drop by drop. The temperature must be held at about 23–27° for the best results. When all this alkaline solution is added the reaction mixture is tested with litmus; if not alkaline, more alkali is added until the neutral point is reached. Upon standing several hours the ester sinks and the alcohol forms the top layer. The alcohol may be siphoned off and used in subsequent experiments, the methyl $p$-toluenesulfonate is washed with water to remove a little salt and then with 5 per cent hydrochloric acid to dissolve the iron. Finally it is

washed with 5 per cent sodium carbonate and water. The ester is then distilled and boils at 161°/10 mm. (m. p. 27–28°). The yield is 90 per cent.

The spent alcohol is distilled from a steam bath, and alcohol of 84–91 per cent purity is obtained which is suitable for subsequent runs.

### 3. Methods of Preparation

Other alkyl esters of arylsulfonic acids have been prepared by this general method.[1] The *n*-butyl ester has been prepared by treating an ethereal solution of *p*-toluenesulfochloride and butyl alcohol with powdered potassium hydroxide,[2] and by refluxing the acid chloride with a 10 per cent excess of alcohol.[2]

[1] Krafft and Roos, Ber. **25**, 2255 (1892); Foldi, Ber. **53**, 1836 (1920); Izmailski and Razorenov, J. Russ. Phys. Chem. Soc. **52**, 359 (1920), [C. A. **18**, 1481 (1924)].

[2] Gilman and Beaber, J. Am. Chem. Soc. **47**, 518 (1925).

X

## *n*-BUTYRYL CHLORIDE

$$CH_3(CH_2)_2CO_2H + SOCl_2 \rightarrow CH_3(CH_2)_2COCl + HCl + SO_2$$

Submitted by B. HELFERICH and W. SCHAEFER.
Checked by HENRY GILMAN and S. A. HARRIS.

### 1. Procedure

IN a 125-cc. distilling flask, provided with a water-cooled side arm to act as reflux condenser (Note 1), is placed 56 g. (0.47 mole) of thionyl chloride (Note 2). This is heated on a water-bath and to it is added during the course of an hour 35.2 g. (0.4 mole) of *n*-butyric acid (Note 3) by means of a separatory funnel attached to the neck of the flask. The evolved gases are absorbed in water.

When all the acid has been added, the mixture is heated for one-half hour on the water bath and then distilled directly from an oil bath into a second distilling flask. The crude acid chloride thus obtained boils between 70–110°; it is purified by distillation through a column and boils almost entirely at 100–101°, only a few drops of forerun being obtained. The yield is 36 g. (85 per cent of the theoretical amount).

### 2. Notes

1. If a Claisen distilling flask is used for the preparation of the acid chloride the side-arm is plugged; the short neck holds the reflux condenser, and the long neck the separatory funnel.

2. The yield is influenced by the purity of the thionyl chloride; the results reported above were obtained with a pure product which boiled over a two-degree range.

3. The presence of traces of water in the butyric acid is of no disadvantage if a correspondingly larger quantity (1 mole for 1 mole of water) of thionyl chloride is used.

## 3. Methods of Preparation

*n*-Butyryl chloride has been prepared from *n*-butyric acid and phosphorus trichloride.[1]

[1] Burcker, Ann. chim. phys. (5) **26**, 468 (1882).

# *o*-CHLOROBENZOYL CHLORIDE

$$o\text{-}ClC_6H_4CHO + Cl_2 \rightarrow o\text{-}ClC_6H_4COCl + HCl$$

Submitted by H. T. Clarke and E. R. Taylor.
Checked by F. C. Whitmore and H. H. Rowley.

## 1. Procedure

In a 3-l. round-bottom flask, fitted with a thermometer, a reflux condenser, and an inlet tube extending nearly to the bottom, is placed 141 g. (1 mole) of freshly distilled *o*-chlorobenzaldehyde (Note 1). To the upper end of the condenser is attached a tube leading to a flask containing water for the absorption of hydrogen chloride. The reaction vessel and absorption flask are accurately weighed, and a current of chlorine, dried by sulfuric acid, is passed into the aldehyde, the temperature of which is maintained at 140–160°. The rate of the current of gas is so regulated that little or no chlorine escapes. The reaction and absorption flasks are removed and weighed about every three hours. After about fifteen hours (Note 2) the absorption of chlorine at 160° practically ceases. The total increase in weight (Note 3) amounts to 26–29 g. (75–84 per cent of the theoretical amount). The reaction product is distilled under reduced pressure, when the pure *o*-chlorobenzoyl chloride passes over at 93–95°/10 mm. or 137–139°/60 mm., leaving a small quantity of high boiling residue which appears to consist mainly of an intermediate compound (Note 2). The yield is 122–126 g. (70–72 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. Technical *o*-chlorobenzaldehyde of high purity is available. After one distillation under reduced pressure (b. p. 84°/10 mm., 125°/85 mm.), it melts at 7–10°.

2. If the mixture be kept at 125–140°, the reaction requires about thirty hours for completion. When about one-half of the necessary amount of chlorine has been added, the reaction mixture, if allowed to cool, sets to a colorless mass of an addition compound of the aldehyde and acid chloride; this on further chlorination yields *o*-chlorobenzoyl chloride.

3. The increase in weight is distributed between the reaction flask and hydrochloric acid absorption flask in the ratio of about 45 : 55.

4. The use of large quantities and vigorous mechanical stirring gives much better yields. Thus, a run of 2665 g. (18.9 moles) of the aldehyde gave a yield of 2700 g. (81 per cent of the theoretical amount).

## 3. Methods of Preparation

The only practical methods for the preparation of *o*-chloro benzoyl chloride to be found in the literature consist in the treatment of *o*-chlorobenzoic acid with phosphorus pentachloride[1] or thionyl chloride.[2] It has, however, also been formed by distilling salicylic acid or its sodium salt with phosphorus pentachloride,[3] and by heating the dichloride of *o*-sulfobenzoic acid.[4]

[1] Emmerling, Ber. **8**, 883 (1875).

[2] H. Meyer, Monatsh. **22**, 427 (1901); Frankland, Carter and Adams, J. Chem. Soc. **101**, 2476 (1912).

[3] Chiozza, Ann. **83**, 317 (1852); Kolbe and Lautemann, Ann. **115**, 183 (1860); Reichenbach and Beilstein, Ann. **132**, 311 (1864).

[4] Remsen and Kohler, Amer. Chem. J. **17**, 332 (1895); Fritsch, Ber. **29**, 2299 (1896); List and Stein, Ber. **31**, 1653 (1898).

# XII

## CYANOACETAMIDE

$$CNCH_2CO_2C_2H_5 + NH_3 \rightarrow CNCH_2CONH_2 + C_2H_5OH$$

Submitted by B. B. Corson, R. W. Scott, and C. E. Vose.
Checked by C. S. Marvel and L. H. Bock.

### 1. Procedure

Four hundred grams (3.5 moles) of ethyl cyanoacetate (Org. Syn. 3, 53; 8, 74) is poured into 300 cc. (4.5 moles) of concentrated aqueous ammonia (sp. gr. 0.90) (Note 1) contained in a 1-l. wide-mouth Erlenmeyer flask. The mixture, which is cloudy at first, is shaken; it then warms up a little and becomes clear in about three minutes. The flask is allowed to stand one hour in an ice-salt mixture. The product is then filtered by suction (Note 2) and the solid washed with two 50-cc. portions of ice-cold ethyl alcohol (Note 3). After drying in the air, the slightly yellowish, crystalline amide weighs 205–225 g. A snow-white product is easily obtained by crystallizing from hot alcohol (Notes 4 and 5). For this purpose 200 g. of amide is dissolved in 350 cc. (Note 6) of hot alcohol and the solution cooled; pure amide is deposited with practically no loss.

An additional yield of amide is obtained by evaporating (Note 7) the original mother liquor to dryness in a vacuum while heating the flask in a boiling water bath. The damp, brownish residue in the flask is dissolved in 100 cc. of hot alcohol. The hot solution is shaken a few minutes with decolorizing charcoal, filtered by suction while still hot, and then cooled in ice. Forty-six to fifty-eight grams of yellowish amide is deposited. One more crystallization with charcoal yields 44–56 g. of pure product.

The total yield is 255–261 g. (86–88 per cent of the theoretical amount). The product melts at 119–120°.

## 2. Notes

1. Gaseous ammonia was tried with poor success, the ammonia being passed into the ester (both cold and at room temperature) and also into an alcoholic solution of the ester.

2. The product must be filtered rapidly while the mother liquor is cold because of the solubility of the amide.

3. Cyanoacetamide may be washed with ice water but cold alcohol is preferable because of its lower solubility in the latter.

4. The solubility of cyanoacetamide in 100 cc. of 95 per cent alcohol follows:

| | |
|---|---|
| 1.3 g. at 0° | 9.5 g. at 52° |
| 1.7 g. at 12° | 14.0 g. at 62° |
| 3.1 g. at 26° | 16.3 g. at 66° |
| 5.0 g. at 38° | 18.7 g. at 69° |
| 7.0 g. at 44° | 21.5 g. at 71° |

5. The alcoholic mother liquor from the crystallization usually contains a small amount of malonamide which melts at 170–171°.

6. If the treatment with decolorizing charcoal is necessary, about 450 cc. of alcohol should be used in order to avoid crystallization during the filtration.

7. A few cubic centimeters of an oil, presumably unchanged ethyl cyanoacetate, comes over with the water.

8. This work was done with the aid of a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

## 3. Methods of Preparation

Cyanoacetamide has been prepared only by the action of aqueous [1] or alcoholic [2] ammonia on cyanoacetic ester.

[1] Van't Hoff, Ber. **7**, 1383 (1874); Henry, Bull. soc. chim. (2) **48**, 656 (1887); Hesse, Amer. Chem. J. **18**, 724 (1896); Thole and Thorpe, J. Chem. Soc. **99**, 429 (1911).

[2] Hesse, Am. Chem. J. **18**, 724 (1896); Ott and Löpmann, Ber. **55**, 1258 (1922).

## ETHYL CINNAMATE

$$C_6H_5CHO + CH_3CO_2C_2H_5 \xrightarrow{(C_2H_5ONa)} C_6H_5CH{=}CHCO_2C_2H_5 + H_2O$$

Submitted by C. S. MARVEL and W. B. KING.
Checked by HENRY GILMAN, R. E. FOTHERGILL, and R. E. BROWN.

### 1. Preparation

IN a 2-l. two-neck flask fitted with a short reflux condenser and mechanical stirrer (Note 1) are placed 400 cc. of dry xylene (Note 2) and 29 g. (1.26 moles) of clean sodium (Note 3) cut in small pieces. The flask is surrounded by an oil-bath and heated until the sodium has melted. At this point the stirrer is started and the sodium is broken up into very small particles (Note 4). The oil-bath is removed but stirring is continued until the sodium has solidified as very fine particles. The xylene is then poured off, and to the sodium is added 455 cc. (4.7 moles) of absolute ethyl acetate (Note 5) containing 3–4 cc. of absolute ethyl alcohol (Note 6). The flask is quickly cooled to 0° and 106 g. (1 mole) of pure benzaldehyde (Note 7) is added slowly from a separatory funnel while the mixture is stirred. The temperature is held between 0° and 5° (Note 8). The reaction starts as soon as the benzaldehyde is added, as is shown by the production of a reddish substance on the particles of the sodium. About one and a half to two hours are required for this addition. The stirring is continued until practically all of the sodium has reacted (one hour after all the aldehyde has been added). When most of the sodium (Note 9) has disappeared, 90–95 cc. of glacial acetic acid is added and the mixture is carefully diluted with

water. The ester layer is separated, the water layer is extracted with about 25–50 cc. of ethyl acetate, and the combined ester portions are washed with 300 cc. of 6 N hydrochloric acid and then dried with sodium sulfate. The ethyl acetate is distilled from a water-bath and the remaining liquid is transferred to a Claisen flask and distilled from an oil-bath under reduced pressure. A small fraction comes over below 128°/6 mm. and is discarded. The ethyl cinnamate (Note 10) boils at 128–133°/6 mm.; 168–173°/46 mm. The yield is 120–130 g. (68–74 per cent of the theoretical amount).

## 2. Notes

1. The stirrer must be very efficient in order to powder the sodium without splashing it onto the walls of the flask above the solvent.

2. The use of sodium powdered under xylene allows the reaction to be carried out much more rapidly than is the case if the sodium is cut into small pieces with a knife. Toluene may be used in place of xylene. The sodium should be as free as possible from oxide.

3. To obtain the maximum yield it is necessary to use slightly more than one equivalent of sodium. When exactly one equivalent is used the yield is about 60 per cent of the theoretical amount.

4. The powdered sodium may also be prepared by melting the sodium under hot xylene and shaking in a tightly stoppered flask wrapped in a heavy cloth.

5. The grade of ethyl acetate used in the preparation is very important. The absolute ethyl acetate (99.7 per cent) sold by the U. S. Industrial Alcohol Company is very satisfactory. If this grade is not available the ordinary ester may be purified by washing first with sodium carbonate solution, then with saturated calcium chloride solution and finally drying over anhydrous potassium carbonate.

6. A small amount of absolute alcohol is needed to start the reaction. When no alcohol is added the yields are consistently

55–60 per cent of the theoretical amount. When too much alcohol (10–15 cc.) is added the yields drop again.

7. Technical benzaldehyde is washed with sodium carbonate and distilled in a vacuum before use. The material used in checking these directions boiled over a 3° range.

8. The temperature should never be allowed to go above 10° and the best yields of pure product are obtained when the temperature is kept within the limits mentioned in the procedure.

9. Usually during the reaction a certain amount of sodium is thrown on the upper part of the flask out of the reaction mixture and forms a cake. In decomposing the mixture with glacial acetic acid and water care must be taken that this sodium does not react violently and thus cause a fire.

10. During the distillation of the ester a reddish semi-solid mass sometimes appears in the flask. This mass melts down if the oil bath is heated to 220–230° and the distillation continues smoothly.

## 3. Methods of Preparation

Ethyl cinnamate occurs in small amounts in storax.[1] It has been prepared by the action of ethyl alcohol on cinnamic acid in the presence of dry hydrochloric or sulfuric acid;[2] by the distillation of the copper salt of the monoethyl ester of benzylidene oxalacetic acid[3] and by the condensation of ethyl acetate and benzaldehyde in the presence of sodium.[4] The method described in the procedure is a slight modification of the one originally described by Claisen.[5]

[1] Miller, Ann. **188**, 203 (1877).

[2] Kopp, Ann. **95**, 318 (1855); Weger, Ann. **221**, 75 (1884); Brühl, Ann. **235**, 19 (1886); Fischer and Speier, Ber. **28**, 3254 (1895).

[3] Wislicenus and Jensen, Ber. **25**, 3449 (1892).

[4] Claisen, Ber. **23**, 977 (1890); Stoermer and Kippe, Ber. **38**, 3034 (1905).

[5] Claisen, Ber. **23**, 977 (1890).

XIV

# HYDROCINNAMIC ACID

$$C_6H_5CH{=}CHCO_2Na + 2H(\text{electrolytic}) \rightarrow C_6H_5CH_2CH_2CO_2Na$$

$$2C_6H_5CH_2CH_2CO_2Na + H_2SO_4 \rightarrow C_6H_5CH_2CH_2CO_2H + Na_2SO_4$$

Submitted by A. W. Ingersoll.
Checked by Henry Gilman and L. C. Heckert.

## 1. Procedure

A. *Apparatus:*

The reduction is carried out in a 7 × 10-inch battery jar (Note 1) which is surrounded by a vessel of cold water. The bottom of the battery jar is just covered with mercury which serves as the cathode of the cell. The anode is a coil of heavy sheet lead separated from the catholyte by suspending it in a porous cup. The latter is supported in the battery jar so that it just clears the surface of the mercury (Note 2). The cathode is connected with the circuit by means of a copper wire well insulated with rubber except for one-eighth inch at the end which is immersed in the mercury. Efficient mechanical stirring is provided for the catholyte. The current used for these experiments was drawn from a storage battery delivering 30 volts, through a rheostat and ammeter each capable of carrying 15 amperes. Current may be taken from any source which will supply 80 to 85 ampere-hours at the rate of 5 to 10 amperes. Several reduction cells of the size described may be run at one time by connecting them in series. The diagram given in Org. Syn. 5, 94 shows the arrangement of the apparatus.

B. *Reduction of Cinnamic Acid:*

After the apparatus is assembled, 2 l. of 7–8 per cent sodium sulfate solution (Note 3) is placed in the battery jar and the porous cup is filled to the same level with more of this solution. The stirrer is started and 200 g. (1.35 moles) of a good grade of cinnamic acid (Note 4) is suspended in the catholyte. A solution of 35 g. (0.88 mole) of sodium hydroxide in 150 cc. of water is then added at such a rate as to avoid forming lumps of sodium cinnamate (Note 5). The current is turned on and the rheostat adjusted until a steady current of 5 to 10 amperes is flowing (Note 6). From this point only occasional attention is required. The suspended sodium cinnamate and cinnamic acid gradually dissolve as the reduction proceeds. Portions adhering to the walls of the cell should be worked down with a stirring rod and finally with a little water from a wash-bottle. The liquor inside the porous cup should be kept alkaline by adding very concentrated sodium hydroxide solution at about half-hour intervals (Note 5). About 110 g. (2.7 moles) will be required. The reduction will require 76 to 80 ampere-hours (Note 7); considerable hydrogen is evolved near the end. The temperature need not be controlled (Note 8).

When reduction is complete (Note 7) the cathode liquor is decanted or siphoned from the mercury, filtered from traces of solid matter and acidified with an excess of sulfuric acid (sp. gr. 1.1). The hydrocinnamic acid separates as an oil and solidifies on thorough cooling. The yield of crude product, which contains water and other impurities is 180–200 g. It is purified by distillation under reduced pressure. The product boiling at 194–197°/75 mm. (145–147°/18 mm.) is colorless and melts at 47.5–48°. The yield of distilled acid is 160–180 g. (80–90 per cent of the theoretical amount) depending upon the quality of the cinnamic acid used (Note 4).

## 2. Notes

1. This is a commercial size. Any sturdy glass vessel of similar dimensions may be used.

2. The lead anode should have about the same surface area as the cathode. The porous cup used was 8 × 21 cm., but similar sizes will do. A three-legged desiccator plate makes a convenient support for the cup.

3. Any dilute solution of sodium sulfate may be used. If several runs are to be made, the solution recovered from the filtration of the hydrocinnamic acid should be neutralized with sodium hydroxide, diluted if necessary, and used again. Traces of hydrocinnamic acid contained in this solution are thus saved. C. P. chemicals are not necessary.

4. The quality of the cinnamic acid used is important. The yield from a commercial C. P. acid melting at 132.5–133° was 86–90 per cent. From a lot melting at 131.5–133° obtained by recrystallizing a crude acid with the use of boneblack the yield was 81–83 per cent. With a technical grade of material the yield fell, in some runs, below 60 per cent, the reduction mixture foamed considerably and much high-boiling residue was left on distillation.

5. The addition of too much sodium hydroxide at this point produces a thick sludge which does not stir well. It should be noted that during the reduction two molecular equivalents of sodium hydroxide are produced at the cathode and an equivalent amount of sulfuric acid at the anode.

6. The current may vary somewhat, especially if the anode liquor becomes too dilute or highly acid. The sodium hydroxide solution added to the anolyte should be concentrated so that the diffusion which always occurs will not dilute the catholyte excessively. High amperage shortens the time required but promotes heating. Seven amperes is a convenient rate.

7. The theoretical quantity of current is 72 ampere-hours. It is necessary to pass an excess of 4 to 8 ampere-hours to insure complete reduction. The end of the reduction is reached when a sample of the catholyte on acidification with excess sulfuric acid precipitates an oil and no solid.

8. The reaction is favored by moderately high temperatures. Excessive heating may be avoided by reducing the amperage or by placing cold water in the cooling bath.

9. It may be noted that this process is essentially a sodium amalgam reduction. By the same procedure β-furylacrylic acid was reduced to β-furylpropionic in yields of 60–70 per cent. With suitable modifications it may be applied to the reduction of other substances reducible with sodium amalgam.

### 3. Methods of Preparation

Hydrocinnamic acid has been prepared by the reduction of cinnamic acid with sodium amalgam,[1] with hydriodic acid at 100°,[2] and with phosphorus and hydriodic acid;[3] by the action of potassium cyanide on β-phenylethyl chloride followed by hydrolysis;[4] by the acid hydrolysis of benzyl-acetoacetic ester;[5] and by several other methods of no preparative value. It has also been prepared electrolytically by the reduction of cinnamic acid in alkaline solution on cathodes of lead[8] and mercury.[9]

[1] Erlenmeyer and Alexejeff, Ann. **121**, 375 (1862).
[2] Glaser, Zeit. f. Chem., **1865**, 111.
[3] Gabriel and Zimmerman, Ber. **13**, 1680 (1880).
[4] Fittig and Kiesow, Ann. **156**, 249 (1870).
[5] Merz and Weith, Ber. **10**, 758 (1877).
[6] Conrad, Ann. **204**, 176 (1880).
[7] Conrad and Hodgkinson, Ann. **193**, 302 (1878).
[8] Norris and Cummings, J. Ind. Eng. Chem. **17**, 305 (1925).
[9] Marie, Compt. rend, **136**, 1331 (1903).

XV

## IODOBENZENE

$$2C_6H_6 + I_2 + [O] (HNO_3) \rightarrow 2C_6H_5I + H_2O$$

Submitted by F. B. Dains and R. Q. Brewster.
Check by Henry Gilman and J. Robinson.

### 1. Procedure

In a 1-l. three-neck flask fitted with a mechanical stirrer, reflux condenser and separatory funnel, are placed 381 g. (1.5 moles) of iodine and 400 g. (5.1 moles) of benzene. The mixture is heated to about 50° on a water bath and 275 cc. of nitric acid (sp. gr. 1.50) is added slowly from the separatory funnel; the time required for the addition should be about one and one-quarter hours. A copious evolution of oxides of nitrogen takes place, and the gases are carried off from the upper end of the condenser to an open window or hood. The reaction proceeds smoothly (Note 1) and the temperature rises slowly without the application of heat until the mixture boils gently. When all of the nitric acid has been added, the solution is refluxed for about fifteen minutes. If iodine still remains, more nitric acid should be added slowly to the warm solution until the purple color of the iodine has been discharged and the solution becomes brownish red.

The lower reddish oily layer is separated, mixed with an equal volume of 10 per cent sodium hydroxide solution and steam distilled from a 2-l. flask until no more oil passes over. Towards the end of the distillation a yellow solid begins to collect in the receiver; this consists of nitro compounds, which are removed by vigorously stirring the oil for about three hours with 20 cc. of concentrated hydrochloric acid, 300 cc. of water and 200 g. of iron filings in a 2-l. flask connected with a reflux condenser.

The mixture is allowed to cool and is then filtered. The filtrate is rendered distinctly acid to congo red with hydrochloric acid and again distilled with steam. The oil so obtained is separated and distilled under normal pressure with the use of a fractionating column (Note 2). The fraction boiling at 180–190° is redistilled and the pure compound is collected at 184–186°. The yield is 523–531 g. (86–87 per cent of the theoretical amount) (Note 3).

## 2. Notes

1. The reaction proceeds smoothly without stirring; however, the time of addition is decreased somewhat by stirring. Ordinary rubber stoppers may be used; although they are somewhat attacked, this is not sufficiently serious to warrant any special apparatus. In very large runs it may be desirable to use stoppers made from asbestos paper and water glass (Org. Syn. 5, 9). Rubber stoppers have been used in a run five times the size of that described.

2. A good separation is obtained by means of a 500-cc. modified Claisen flask (Org. Syn. 1, 40) without the use of diminished pressure.

3. Iodobenzene prepared by this procedure may contain traces of nitro compounds. The test for these is to reduce a sample with stannous chloride (or tin) and hydrochloric acid, and treat the resulting acid solution in the cold with a solution of sodium nitrite. If a phenolic odor is obtained on boiling the solution, nitro compounds are still present. A more delicate test can be made by adding the reduced solution, after treatment with sodium nitrite, to an alkaline solution of $\beta$-naphthol; an azo dye is formed if nitro compounds were originally present.

## 3. Methods of Preparation

The present method is essentially that of Datta and Chatterjee.[1] Oxidizing agents other than nitric acid have been used in the preparation of iodobenzene from benzene and iodine, but

[1] Datta and Chatterjee, J. Am. Chem. Soc. **39**, 437 (1917).

no one of them appears to be as effective and as convenient as nitric acid. Those that have been used are iodic acid,[2] fuming sulfuric acid,[3] mercuric oxide[4] and ferric chloride.[5] Other methods of preparative interest are the diazo reaction starting with aniline;[6] the reaction between benzene, iodine monochloride and aluminum chloride;[7] benzene, sulfur iodide and nitric acid;[8] and phenylmagnesium bromide and iodine.[9]

[2] Kekulé, Ann. **137**, 162 (1866); Klages and Liecke, J. prakt. chem. (2) **61**, 311 (1900).

[3] Rupp, Ber. **29**, 1629 (1896); Neumann, Ann. **241**, 84 (1887).

[4] Weselsky, Ann. **174**, 99 (1874).

[5] Meyer, Ann. **231**, 195 (1885); J. prakt. Chem. (2) **34**, 504 (1886).

[6] Griess, Jahresber. **1866**, p. 477.

[7] Greene, Bull. soc. chim. **36**, 234 (1881).

[8] Edinger and Goldberg, Ber. **33**, 2875 (1900).

[9] Datta and Mitter, J. Am. Chem. Soc. **41**, 288 (1919).

XVI

# LEVULINIC ACID

$$C_{12}H_{22}O_{11} \rightarrow 2CH_3COCH_2CH_2CO_2H + 2HCO_2H + H_2O$$

Submitted by B. F. McKenzie.
Checked by H. T. Clarke and R. Phillips.

## 1. Procedure

To a solution of 500 g. (1.46 moles) of cane sugar (Note 1) in 1 l. of water in a 2-l. flask is added 250 cc. of concentrated hydrochloric acid (sp. gr. 1.16). The flask is heated on a steam-bath for twenty-four hours, during which time considerable carbonization takes place. The black solid is filtered off with suction and washed with 300 cc. of water. The filtrate is placed in a large evaporating dish on a steam-bath and allowed to evaporate overnight. The black solid residue obtained on the following morning is ground to a powder and placed in a folded filter paper of 34 cm. diameter. This is placed in a 25-cm. funnel fitted with a water-cooled 12-l. flask as described in Org. Syn. **2**, 49. The solid is extracted with 500 cc. of ether for six to eight hours. The ether is distilled and the residue (Note 2) fractionated under reduced pressure. The fraction distilling at 150–160°/15 mm. or 135–140°/10 mm. forms a rather dark liquid which does not completely solidify on cooling.

On redistillation under reduced pressure a fraction boiling over a range of not more than 2° (e.g., 137–139°/10 mm.) is obtained with very little loss; this fraction solidifies almost completely at 30°. The yield is 72–76 g. (22–23 per cent of the theoretical amount).

## 2. Notes

1. Equally good results may be obtained with starch; the mixture, however, must be warmed more slowly as it is apt to foam at the outset.

2. When larger quantities of levulinic acid are to be prepared it has been found by the checkers to be more convenient to fractionally distil the first filtrate under reduced pressure, without evaporating to dryness and extracting with ether. In this case a considerable quantity of tarry residue remains in the distilling flask. The yields are equally good.

### 3. Methods of Preparation

*The only practical methods for preparing levulinic acid depend* upon the action of mineral acids upon carbohydrates, a reaction discovered by Grote and Tollens,[1] who heated cane sugar with dilute sulfuric acid. The method above described is essentially that of Conrad,[2] descriptions of which frequently have appeared [3] in the subsequent literature. The use of vacuum distillation was suggested by Kent and Tollens.[4] Levulinic acid has also been prepared from starch by the action of hydrochloric acid.[5]

[1] Grote and Tollens, Ann. **175**, 181 (1875); **206**, 226 (1880).

[2] Conrad, Ber. **11**, 2177 (1878).

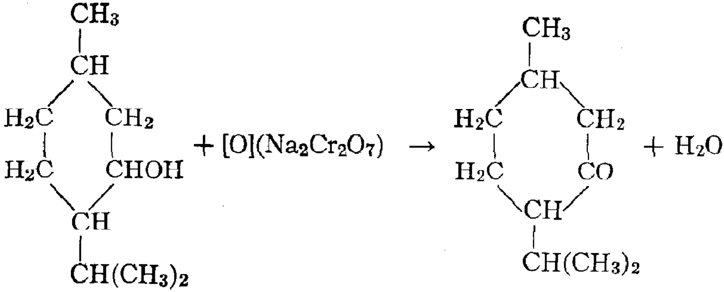
[3] Fittig and Wolff, Ann. **208**, 104 (1881); Neugebauer, Ann. **227**, 97 (1885); Seissl, Ann. **249**, 272 (1888).

[4] Kent and Tollens, Ann. **227**, 229, Note 2 (1885).

[5] Rischbieth, Ber. **20**, 1773 (1887).

# XVII

## *l*-MENTHONE



Submitted by L. T. SANDBORN.
Checked by H. T. CLARKE and ROSS PHILLIPS.

### 1. Procedure

IN a 1-l. round-bottom flask provided with a mechanical stirrer is placed 120 g. (0.4 mole) of crystallized sodium dichromate (or an equivalent amount of potassium dichromate), and to this is added a solution of 100 g. (0.97 mole) of concentrated sulphuric acid (sp. gr. 1.84) in 600 cc. of water. To this mixture 90 g. (0.57 mole) of menthol (crystals, m. p. 41–42°) is added in three or four portions and the mixture stirred (Note 1). Heat is evolved and the temperature of the mixture rises to about 55° (Note 2). As soon as the reaction is complete the temperature falls. The oil is mixed with an equal volume of ether, separated in a separatory funnel, and washed with three 200-cc. portions of 5 per cent sodium hydroxide solution (Note 3). The ether is then removed by distillation and the residue distilled under reduced pressure, the menthone being collected at 98–100°/18 mm. If distilled under atmospheric pressure it boils at 204–207°. The yield is 74–76 g. (83–85 per cent of the theoretical amount).

## 2. Notes

1. On addition of the menthol a black spongy mass forms which softens as the temperature rises and finally forms a dark-brown oil.

2. The temperature may not reach 55°, in which case the mixture may be warmed gently with a small flame. In case the reaction is slow in starting, gentle heating with a small flame is advantageous.

3. The oil, which is dark brown before washing with sodium hydroxide, becomes light yellow. If three washings are not sufficient to remove the dark color another portion of sodium hydroxide solution is used.

## 3. Methods of Preparation

*l*-Menthone can be made by the oxidation of rhodinol with a chromic-sulphuric acid mixture.[1] A Sabatier–Senderens reduction of thymol gives a mixture containing 30 per cent menthone.[2] *l*-Menthone is also obtained by treating menthol with copper at 300°.[3] The method used in these directions is that of Beckmann.[4]

[1] Bouveault, Bull. soc. chim. (3) **23**, 464 (1900).

[2] Pickard and Littlebury, J. Chem. Soc. **101**, 113 (1912).

[3] Neave, J. Chem. Soc. **101**, 513 (1912).

[4] Beckmann, Ann. **250**, 325 (1889).

XVIII

## MERCURY DIPHENYL

$$2\ C_6H_5Br + Na_2Hg \rightarrow (C_6H_5)_2Hg + 2NaBr$$

Submitted by H. O. CALVERY.
Checked by FRANK C. WHITMORE and R. W. BEATTIE.

### 1. Procedure

IN a 1-l. round-bottom flask fitted with a reflux condenser are placed 900 g. of 3 per cent sodium amalgam (Note 1), 180 g. (1.15 moles) of bromobenzene, 200 cc. of dry toluene or dry xylene, and 10 cc. of ethyl acetate. The mixture is refluxed with frequent shaking for twelve hours in an oil bath at 130°.

The mixture is transferred (Hood) (Note 5) while still hot to a a fluted filter paper in a 20-cm. glass funnel, leaving behind as much mercury as possible (Note 2). The funnel is made part of a special extraction apparatus as described in Org. Syn. **2**, 49. The mercury diphenyl is extracted with 600 cc. of boiling benzene for about ten hours (Note 3).

The solution is distilled under reduced pressure on an oil bath, the temperature of which is raised to 110° near the end of the distillation. The solid residue left in the flask after removal of the solvent is taken out and washed until nearly white with 95 per cent alcohol which has been cooled in an ice bath. This requires about four washings of 50 cc. of alcohol each (Note 4). The yield is 65–75 g. (32–37 per cent of the theoretical amount). The melting point is 121–123°.

### 2. Notes

1. For the preparation of sodium amalgam see Org. Syn. **7**, 89.
2. Care must be taken to remove all the mercury diphenyl;

but if too much mercury is removed, it may break the filter paper or weight it down so that the benzene vapors cannot rise around it. It is sometimes best to put stirring rods down around the sides of the paper to insure a free path for the benzene vapors.

3. In some cases the extraction may not be complete in this length of time.

4. Some mercury diphenyl may be recovered by combining the washings from several runs.

5. Mercury diphenyl is very poisonous. The vapors of the benzene solution must not be breathed.

## 3. Methods of Preparation

Mercury diphenyl has been prepared in a number of ways. The most important methods are: by the action of sodium on a mixture of bromobenzene and mercuric chloride;[1] from sodium amalgam and phenyl mercuric iodide;[2] by the interaction of phenyl mercuric bromide and potassium sulfide[2] or phenyl mercuric acetate and sodium stannite;[3] from phenyl magnesium bromide and mercuric chloride;[4] by the action of phenyl hydrazine on mercury compounds;[5] from mercuric chloride and phenyl arsenious oxide;[6] and from diphenyl mercuric ammonium acetate and sulfur compounds.[7]

[1] Michaelis and Reese, Ber. **15**, 2877 (1882).
[2] Dreher and Otto, Ber. **2**, 542 (1869).
[3] Dimroth, Ber. **35**, 2853 (1902).
[4] Pfeiffer and Truskier, Ber. **37**, 1127 (1904).
[5] Fischer and Erhardt, Ann. **199**, 332 (1879).
[6] Fraenkel, Arzneimittelsynthese, 4th ed. (1919), 661.
[7] Pesci, Gazz. chim. ital. **39**, I, 150 (1909).

XIX

# METHYLENE BROMIDE

$$CHBr_3 + NaOH + Na_3AsO_3 \rightarrow CH_2Br_2 + Na_3AsO_4 + NaBr$$

Submitted by W. W. Hartman and E. E. Dreger.
Checked by Frank C. Whitmore and C. J. Korpi.

## 1. Procedure

In a 2-l. round-bottom flask placed on a steam bath and fitted with a stirrer, a separatory funnel, and a reflux condenser is placed 540 g. (1.9 moles) of commercial (88 per cent) bromoform (Note 1). There is then added 10 cc. of a solution of sodium arsenite made by dissolving 230 g. (1.16 moles) of c. p. arsenious oxide and 445 g. (11 moles) of sodium hydroxide in 1.4 l. of water. The mixture is warmed gently to start the reaction, and then the remainder of the sodium arsenite solution is added during about one hour at such a rate that the solution refluxes gently. When the addition is complete, the flask is heated for four hours on the steam bath. The reaction mixture is distilled with steam, the lower layer of methylene bromide separated, and the water layer extracted once with 100 cc. of ether (Note 2). The methylene bromide is dried with 10 g. of calcium chloride and distilled. The yield of slightly yellow liquid boiling at 97–100° is 290–300 g. (88–90 per cent of the theoretical amount).

## 2. Notes

1. The commercial bromoform used contained 12 per cent of alcohol. Its specific gravity was 2.59/25° as compared with 2.88/25° for pure bromoform.

2. The chief function of the extraction is to collect the fine droplets of methylene bromide which remain in the water layer.

## 3. Methods of Preparation

Methylene bromide has been prepared by the reaction of bromine with methylene iodide,[1] and by the action of bromine on methyl bromide[2] at 250°. The present method is adapted from the preparation of methylene iodide described in Org. Syn. 1, 57.

[1] Butlerow, Ann. **111**, 251 (1859).

[2] Steiner, Ber. **7**, 507 (1874).

XX

## MONOCHLOROMETHYL ETHER

$$HCHO+CH_3OH+HCl \rightarrow ClCH_2OCH_3+H_2O$$

Submitted by C. S. Marvel and P. K. Porter.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure

In a 2-l. round-bottom flask fitted with a stopper carrying a reflux condenser and a glass tube reaching nearly to the bottom of the flask are placed 350 g. (10.9 moles) of methyl alcohol and 900 g. of technical formalin containing 252 g. (8.4 moles) of formaldehyde (Note 1).

A rapid stream of hydrogen chloride (Note 2) is run into the mixture, which is cooled with running water. In about two hours a layer of chloromethyl ether begins to appear. The stream of hydrogen chloride is continued for two or three hours longer until the solution is saturated. The layer of chloromethyl ether is then separated. The water layer is saturated with calcium chloride (Note 3) and more ether separates. This is added to the main portion which is then dried over calcium chloride and fractionally distilled. The yield of a product boiling at 55–60° is 580–600 g. (86–89 per cent of the theoretical amount based on the formaldehyde).

### 2. Notes

1. The following table showing the relation between the density of formalin solutions and their formaldehyde content has been found useful. It is copied from Beilstein's Handbuch

der Organischen Chemie, 4th Ed., Julius Springer, Berlin, 1918, Vol. I, page 561.

| $d\frac{18}{4}$ | g. $CH_2O$ in 100 cc. | g. $CH_2O$ in 100 g. |
|---|---|---|
| 1.0054 | 2.24 | 2.23 |
| 1.0126 | 4.66 | 4.60 |
| 1.0311 | 11.08 | 10.74 |
| 1.0410 | 14.15 | 13.59 |
| 1.0568 | 19.89 | 18.82 |
| 1.0719 | 25.44 | 23.73 |
| 1.0853 | 30.17 | 27.80 |
| 1.1057 | 37.72 | 34.11 |
| 1.1158 | 41.87 | 37.53 |

2. The hydrogen chloride was generated by the method described in Org. Syn. **2**, 30. About 390–420 g. of hydrogen chloride is required for saturation.

3. Chloromethyl ether is soluble in the aqueous hydrochloric acid used so that the salting out with calcium chloride is necessary to obtain the maximum yield.

### 3. Methods of Preparation

Monochloromethyl ether has been prepared by saturating an aqueous solution of formaldehyde and methyl alcohol with hydrogen chloride [1] and by saturating a solution of trioxymethylene in methyl alcohol with hydrogen chloride.[2] The method which is described in the procedure is essentially that developed by Henry.[3]

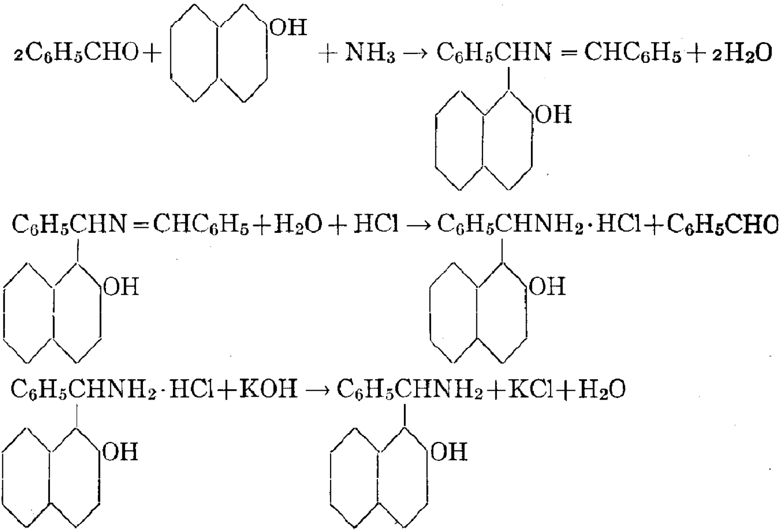
[1] Henry, Ber. **26**, 933 (1893); Favre, Bull. soc. chim. (3) **11**, 1095 (1894); Litterscheid and Thimme, Ann. **334**, 10 (1904).

[2] Wedekind, Ger. pat. 135,310 (Chem. Zentr. **1902** (II), 1164); Ber. **36**, 1384 (1903); Houben and Arnold, Ber. **40**, 4307 (1907); Litterscheid, Ann. **330**, 109 (1904); Reychler, Bull. soc. chim. (4) **1**, 1195 (1907).

[3] Henry, Ber. **26**, 933 (1893).

XXI

## β-NAPHTHOL PHENYLAMINOMETHANE




Submitted by M. Betti.
Checked by C. S. Marvel and G. S. Hiers.

### 1. Procedure

In a 1-l. round-bottom flask is placed a cold solution of 144 g. (1 mole) of β-naphthol in 200 cc. of 95 per cent alcohol (Note 1). To this solution is added first 212 g. (2 moles) of freshly distilled benzaldehyde (which has been previously freed from acid by shaking with 5 per cent sodium carbonate solution) and then about 200 cc. of 95 per cent alcohol which has been saturated with ammonia at room temperature. The solution becomes red and warms up spontaneously. The flask is stoppered and allowed to

stand for two hours. Then the stopper is removed, and the excess ammonia is allowed to escape. After about twelve hours, the condensation product, which has separated as white needles, is filtered with suction and washed with 50 cc. of alcohol. The mother liquors on standing for three days deposit an additional quantity of the condensation product (Note 2). The yield is 284–306 g. (85–92 per cent of the theoretical amount) of a product which melts at 148–150°.

The condensation product thus obtained is introduced into a 5-l. round-bottom flask arranged for steam distillation, and treated with three to four times its volume of 20 per cent hydrochloric acid. The mixture is steam distilled to remove all benzaldehyde formed by the hydrolysis (about two hours) (Note 3). Meanwhile, an abundant flocculent precipitate of light pink or white needles separates. The mixture in the flask is cooled thoroughly and filtered with suction. The yield is 240–260 g. (84–91 per cent of the theoretical amount) of a product which melts at 190–220° with decomposition (Note 4).

The hydrochloride thus obtained varies from pure white to a light red in color, depending on the purity of the original reagents and on the length of time required for the hydrolysis. However, the color does not interfere with isolation of a pure white free base when the salt is treated with alkali. The salt is somewhat more stable than the free base, and if the reagent is to be stored for some time, it should be kept in this form.

In order to obtain the amine, 200 g. of finely divided hydrochloride is placed in a 1500-cc. beaker and stirred into a smooth paste with 300 cc. of water. To this is added 50 g. of crushed ice, and the mixture is cooled in an ice bath (Note 5). Then 750–800 cc. of 25 per cent aqueous potassium hydroxide is added slowly with stirring until the hydrochloride dissolves. The cold solution is transferred to a separatory funnel and extracted with four 300-cc. portions of ether. The combined ether extract is dried overnight with 50 g. of anhydrous sodium sulfate, filtered, and concentrated to about 300 cc. On cooling the solution in an ice bath, the amine crystallizes and is filtered with suction. The first crop of crystals weighs 112–115 g. Further concen-

tration of the mother liquors to about 100 cc. and cooling yields 14–18 g. more of the product (Note 6). The total yield is 127–131 g. (73–75 per cent of the theoretical amount) of a product which melts at 124–125° (Note 7). If desired, it may be purified by dissolving in an excess of dry ether, evaporating the excess of solvent, and allowing the amine to crystallize. Thus, 24.5 g. of the amine, when dissolved in 800 cc. of dry ether and the solution filtered and evaporated in a current of air to 150 cc., yields 18–19 g. of product, melting at 124–125°.

## 2. Notes

1. It is usually necessary to warm the alcohol in order to dissolve the β-naphthol. This solution is then cooled before the addition of the benzaldehyde.

2. Even after three days' standing, the reaction is not entirely complete, and an additional 8–10 g. of product may be obtained by allowing the mother liquors to stand for another three or four days.

3. Sometimes when the distillation is carried on for too long a period, the hydrochloride coagulates to a hard red mass. If this happens, the product may be purified by crystallization from about 15 per cent hydrochloric acid. Even the deeply colored hydrochloride yields a colorless amine.

4. The hydrochloride is almost insoluble in cold water. It is slightly hydrolyzed by boiling water.

5. The temperature should be kept below 20° during the addition of the alkali, or the product is decomposed and ammonia is evolved.

6. A small additional amount of impure product may be obtained by evaporating the mother liquors further and cooling the solution. This product amounts to only a few grams and needs to be purified by recrystallization from ether.

7. This amine is of interest because it is readily resolved with tartaric acid to give the pure dextro and levo isomers.[1]

[1] Betti, Gazz. chim. ital. **36**, **II**, 392 (1906).

These optically active bases are very useful in the resolution of various types of racemic substances.

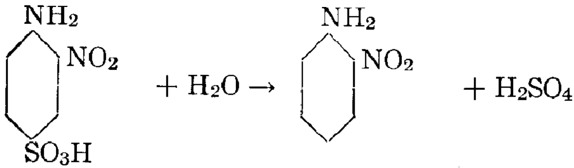
## 3. Methods of Preparation

β-Naphthol phenylaminomethane has been prepared only by the method outlined in the procedure.[2]

[2] Betti, Gazz. chim. ital. **31**, I, 385 (1901).

## XXII

## *o*-NITROANILINE




Submitted by Louis Ehrenfeld and Milton Puterbaugh.
Checked by Roger Adams and S. V. Puntambeker.

### 1. Procedure

In a 3-l. round-bottom flask fitted with a reflux condenser are placed 218 g. (1 mole) of coarsely powdered technical *o*-nitroaniline-*p*-sulfonic acid, and a hot mixture of 775 cc. of concentrated sulfuric acid (sp. gr. 1.84) and 950 cc. of water (Note 1). Heat is applied and the mixture is refluxed gently for an hour after solution is practically complete (total about three hours). The resulting dark solution is allowed to cool and is poured slowly into 12 l. of cold water in a crock (Note 2).

After cooling, the dense orange-yellow precipitate is filtered with suction. This crop of crystals after air-drying weighs about 70 g. and melts at 68–70°. The filtrate is returned to the crock and made slightly alkaline with 50 per cent sodium hydroxide solution (about 2.25 l.). It is then made barely acid to litmus with sulfuric acid. This neutralization will produce considerable heat and the mixture should be thoroughly cooled before filtering. This second crop of crystals weighs about 22–25 g. and melts at 69–70.5°. The total crude yield is 90–95 g.

The two crops of crystals may be combined for recrystallization from boiling water, using 1 l. for each 9 g. The hot solution

is filtered quickly and the filtrate is cooled thoroughly and filtered with suction. The crystals are dried at 50°. The product melts at 69–71°. An alternate method of purification is to dissolve the crude product in about 250 cc. of 95 per cent alcohol, filter the solution, dilute with 1 l. of hot water and warm on a steam bath if a precipitate forms. On cooling this solution the product separates in orange-brown needles, and is filtered and air dried. The yield is about 78 g. (56 per cent of the theoretical amount), m.p. 69.5–70.5°.

## 2. Notes

1. If cold, diluted acid is used, stirring must be employed during the heating to prevent caking and consequent charring.

2. The dark solution may be poured slowly over sufficient ice to half-fill a 16-l. (4-gal.) crock. A good yield was obtained in this way, but at this point the temperature is not likely to rise much and the use of cold water is cheaper and sufficiently satisfactory.

## 3. Methods of Preparation

*o-Nitroaniline has been obtained together with some p*-nitroaniline in the nitration and subsequent hydrolysis of acetanilide [1] and of benzanilide; [2] by the sulfonation, nitration and subsequent hydrolysis of oxanilide [3] and of acetanilide; [4] by the nitration of aniline and separation of the mixture of isomers; [5] and by heating a mixture of *o*-chloronitrobenzene with ammonium acetate.[6]

[1] Walker and Zincke, Ber. **5**, 114 (1872); Remsen and Graham, Am. Chem. J. **11**, 320 (1889); Weida, Am. Chem. J. **19**, 547 (1897); Pokorry, Bull. Soc. Indus. Mulhouse **1894**, 280 [Chem. Zentr. **1894**, II, 556].

[2] Lellmann, Ann. **221**, 6 (1883).

[3] Ger. pat. 65,212; 66,060 [Frdl. **3**, 44, 45 (1892)].

[4] Nietzki and Benckiser, Ber. **18**, 295 (1885); Turner, Ber. **25**, 986 (1892); Sakellarios, Ber. **58**, 2286 (1925).

[5] Bruns, Ber. **28**, 1954 (1895).

[6] Brit. pat. 169,688 [C. A. **16**, 721 (1922)].

XXIII

## NITROSTYRENE

$$C_6H_5CHO + CH_3NO_2 + NaOH \rightarrow C_6H_5CHOHCH{=}NO_2Na$$

$$C_6H_5CHOHCH{=}NO_2Na + HCl \rightarrow C_6H_5CH{=}CHNO_2 + NaCl + H_2O$$

Submitted by DAVID E. WORRALL.
Checked by C. S. MARVEL and W. H. LYCAN.

### 1. Procedure

IN a 6-l. wide-mouth bottle, packed in a pail with a freezing mixture of ice and salt and fitted with a mechanical stirrer, a thermometer and a separatory funnel, are placed 305 g. (5 moles) of nitromethane (Org. Syn. **3**, 83) 530 g. (5 moles) of benzaldehyde (Note 1) and 1000 cc. of methyl alcohol. A solution of sodium hydroxide is prepared by dissolving 210 g. (5.25 moles) of caustic soda in approximately an equal volume of water and cooling. It is then diluted to 500 cc. with ice and water, poured into the funnel, and added with stirring to the nitromethane mixture at such a rate that the temperature is kept at 10–15° (Notes 2 and 3).

A bulky white precipitate forms rapidly during the addition of the alkali. The mixture gets so thick that stirring becomes difficult and it may be advisable to add 100 cc. more of methyl alcohol. After fifteen minutes' standing, the pasty mass is converted to a clear solution by the addition of 3–3.5 l. of ice water containing crushed ice (Note 4). Hydrochloric acid (made by diluting 1000 cc. of concentrated hydrochloric acid with 1500 cc. of water) is placed in a 15-l. mixing jar and the reaction mixture run into this from the separatory funnel at such a rate that the stream just fails to break into drops (Note 5). A pale

yellow crystalline mass separates almost immediately as the alkaline solution comes in contact with the acid. After the stirring is stopped, the solid settles to the bottom of the jar. The major part of the cloudy liquid layer is removed by decantation, and the residue filtered by suction and washed with water until free from chlorides. This product is freed from all but a negligible amount of water by melting in a beaker immersed in hot water. Two layers are formed and on cooling again the lower layer of nitrostyrene freezes; the water may then be poured off. The crude nitrostyrene is purified by dissolving in 420 cc. of hot ethyl alcohol (Note 6), filtering the solution into a warm suction flask to remove solid impurities, and then cooling until crystallization is complete. The yield of crude product melting at 56–58° is 650–670 g. The yield of recrystallized nitrostyrene melting sharply at 57–58° is 600–620 g. (80–83 per cent of the theoretical amount). The whole procedure, including purification, can be done in a day.

## 2. Notes

1. Technical benzaldehyde which had been washed with sodium carbonate solution, dried and distilled under reduced pressure, was used in this preparation.

2. The first few cubic centimeters of sodium hydroxide solution should be added cautiously to the nitromethane mixture since, after a short induction period, there is a considerable evolution of heat and the temperature may rise from −10° to 30° or even higher in spite of good stirring. If necessary, this rise in temperature is easily checked by adding a handful of crushed ice directly to the mixture. After this initial reaction the rest of the alkali may be added more rapidly.

3. The condensation induced by sodium hydroxide is almost instantaneous above 10°. The procedure may be interrupted with safety after the addition of alkali, and the product will not change on standing overnight in an ice chest.

4. After the product has been dissolved in water the resulting alkaline solution is much more sensitive and should be used up as rapidly as possible and the temperature kept below 5°.

5. The alkaline solution must be added slowly to the acid, for the reverse procedure always forms an oil containing a saturated nitro alcohol. A large excess of acid at room temperature is used, conditions which facilitate the formation of the desired unsaturated nitro compound.

6. The vapors of hot solutions of nitrostyrene are very irritating to the eyes and nose, while the skin of the face is sensitive to the solid substance.

### 3. Methods of Preparation

Nitrostyrene has been obtained in small yields by a number of methods, but the only practical methods of preparation start with benzaldehyde and nitromethane. The condensation was first accomplished by heating nitromethane and benzaldehyde in sealed tubes with anhydrous zinc chloride.[1] Good results are obtained by adding small amounts of a primary aliphatic amine to a mixture of nitromethane and benzaldehyde,[2] but it takes a number of days for the reaction to go to completion. Undoubtedly the best method is the use of alkali to condense benzaldehyde and nitromethane, as first discovered by Thiele.[3]

[1] Priebs, Ann. **225**, 320 (1884).

[2] Knoevenagel and Walter, Ber. **37**, 4507 (1904).

[3] Thiele, Ber. **32**, 1293 (1899); Thiele and Haeckel, Ann. **325**, 7 (1902).

XXIV

## PENTAMETHYLENE BROMIDE

$$C_5H_{10}NCOC_6H_5 + PBr_5 \rightarrow Br(CH_2)_5Br + C_6H_5CN + POBr_3$$

Submitted by J. VON BRAUN.
Checked by J. B. CONANT and J. S. ANDREWS.

### 1. Procedure

IN a 500-cc. Claisen distilling flask is placed 80 g. (0.42 mole) of benzoyl piperidine (p. 16). To this is added with cooling 115 g. (0.43 mole) of phosphorus tribromide; this results in the formation of a light-colored solution. With careful cooling, this solution is treated, with shaking, with 65 g. of bromine (0.81 mole). The flask is now connected for vacuum distillation and the solution heated gradually for a few minutes until the rapid evolution of gas ceases. The product is then vacuum distilled. At about 70°/20 mm. a mixture of pentamethylene bromide, phosphorus oxybromide and benzonitrile begins to distil over into the receiver; a yellow solid collects in the condenser. This is then followed by a black decomposition product, at which point the distillation is stopped. The distillate is poured onto ice and allowed to stand in order to decompose the phosphorus oxybromide, a process which requires about one hour if carried out in a flask fitted with a reflux condenser and mechanical stirrer. The heavy oil is removed from the water and consists of pentamethylene bromide and benzonitrile. This oily layer is treated with 125 cc. of 40 per cent hydrobromic acid solution and boiled under a reflux condenser with vigorous stirring for about three hours in order to hydrolyze completely the benzonitrile to benzoic acid (Note 1). The mixture is then distilled with steam using an air condenser between the distillation flask

and the receiving flask and fitting to the latter a reflux condenser cooled with water. This apparatus is necessary to avoid clogging of the condenser tubes with the benzoic acid. The pentamethylene bromide *is separated from the water layer, washed* with sodium carbonate, dried over calcium chloride and distilled under reduced pressure. The product boils at 108–110°/20 mm. and amounts to 63–70 g. (65–72 per cent of the theoretical amount).

## 2. Notes

1. It has been suggested in the literature[1] that the benzonitrile may be removed from the pentamethylene bromide by shaking repeatedly with concentrated sulfuric acid. This did not prove satisfactory in the laboratory on account of the formation of emulsions. When a solvent such as petroleum ether is added, the emulsions may be avoided but the yield of final product is always lower than that obtained by the method described.

## *3. Methods of Preparation*

Pentamethylene bromide has been prepared by the action of fuming hydrobromic acid on pentamethylene glycol,[2] or 1,5-diphenoxypentane;[3] by the action of hydrobromic acid on an acetic acid solution of 1,5-di-isoamyloxypentane;[4] and by the action of phosphorus pentabromide on benzoyl piperidine.[5]

[1] Dox and Yoder, J. Am. Chem. Soc. **43**, 1368 (1921); Clarke, J. Chem. Soc. **103**, 1703 footnote (1913).

[2] Gustavson and Demjanoff, J. prakt. Chem. (2) **39**, 542 (1889); Haworth and Perkin, Ber. **26**, 2247 (1893); Hochstetter, Monatsh. **23**, 1071 (1902).

[3] v. Braun and Steindorff, Ber. **38**, 960 (1905).

[4] Hamonet, Compt. rend. **138**, 1611 (1904); Bull. soc. chim. (3) **33**, 530 (1905).

[5] v. Braun, Ber. **37**, 3211 (1904); J. v. Braun and Steindorff, ibid. **38**, 2338 (1905); Ger. pat. 164, 365 [Chem. Zentr. **1905**, II, 1564]; Clarke, J. Chem. Soc. **103**, 1703 footnote (1913); Dox and Yoder, J. Am. Chem. Soc. **43**, 1368 (1921).

XXV

## γ-PHENOXYPROPYL BROMIDE

$$C_6H_5ONa + BrCH_2CH_2CH_2Br \rightarrow C_6H_5OCH_2CH_2CH_2Br + NaBr$$

Submitted by C. S. Marvel and A. L. Tanenbaum.
Checked by H. T. Clarke and C. J. Malm.

### 1. Procedure

In a 5-l. round-bottom flask, fitted with a stopper carrying a long reflux condenser, a mechanical stirrer (Note 1) and a separatory funnel, are placed 2 l. of water (Note 2), 1 kg. (4.95 moles) of trimethylene bromide (Org. Syn. **1**, 8) (Note 3) and 370 g. (3.9 moles) of phenol. The stirrer is started and the mixture is heated to boiling. To the boiling solution is added a solution of 150 g. (3.75 moles) of sodium hydroxide in 500 cc. of water at such a rate that all is added in about one hour. The mixture is refluxed for five to six hours longer to complete the reaction, then cooled and the upper water layer separated and discarded. The lower layer consists of trimethylene bromide, phenoxypropyl bromide and diphenoxypropane. This mixture is distilled under reduced pressure, using a Claisen flask with a modified side arm (Org. Syn. **1**, 40). The first fraction is collected up to 136°/20 mm. and consists of water and recovered trimethylene bromide with a little phenoxypropyl bromide (Note 4). The water is separated and discarded. The recovered trimethylene bromide weighs 340–450 g. (Note 5). The next fraction is pure phenoxypropyl bromide which boils at 136–142°/20 mm. The yield is 495–600 g. (84–85 per cent of the theoretical amount based on the trimethylene bromide actually used) (Note 6). On cooling the phenoxypropyl bromide, it crystallizes to a white solid, m.p. 7–8°. A small amount (50–

80 g.) of diphenoxypropane is left as a residue in the distilling flask.

## 2. Notes

1. The reaction may be run without stirring but a longer period of refluxing is necessary and the yield is lower.

2. If less water is used in the reaction mixture, sodium bromide separates.

3. The large excess of trimethylene bromide must be used in order to avoid the formation of large amounts of diphenoxypropane.

4. Phenoxypropyl bromide attacks rubber stoppers quite readily and the side arm of the distillation flask should be set in (Org. Syn. 1, 40) in order to avoid contamination of the distillate.

5. The use of recovered trimethylene bromide does not result in as good a yield of phenoxypropyl bromide, because a little phenoxypropyl bromide is already present and during the reaction is converted to diphenoxypropane.

6. Phenoxyethyl bromide may be made in a similar manner. Two kilos of ethylene bromide, 285 g. of phenol and 2 l. of water, upon treatment with 375 g. of sodium hydroxide, yield 960–970 g. of phenoxyethyl bromide (54–57 per cent of the theoretical amount) boiling at 125–130°/18 mm.

## 3. Methods of Preparation

γ-Phenoxypropyl bromide has been prepared by the action of sodium phenoxide on trimethylene bromide in alcohol solution.[1] The method described in the procedure has been published by Marvel and Tanenbaum.[2]

[1] Lohmann, Ber. **24**, 2631 (1891); Salonina, Ber. **26**, 2987 (1893); v. Braun and Beschke, Ber. **39**, 4120 (1906).

[2] Marvel and Tanenbaum, J. Am. Chem. Soc. **44**, 2647 (1922).

## XXVI

## PHLOROGLUCINOL

$$C_6H_2(NO_2)_3CO_2H + 12[H](Sn + HCl) \rightarrow C_6H_2(NH_2)_3CO_2H + 6H_2O$$

$$C_6H_2(NH_2)_3CO_2H + 5H_2O + 3HCl \rightarrow C_6H_3(OH)_3 \cdot 2H_2O + 3NH_4Cl + CO_2$$

Submitted by H. T. CLARKE and W. W. HARTMAN.
Checked by C. S. MARVEL and A. T. BLOMQUIST.

### 1. Procedure

To 225 g. (0.87 mole) of crude 2,4,6-trinitrobenzoic acid (Notes 1 and 2), prepared as described in Org. Syn. **2**, 95, is added 1800 cc. of concentrated hydrochloric acid (sp. gr. 1.17) in a 5-l. flask provided with a reflux condenser, the inner tube of which is 15–20 mm. in diameter. To this mixture is added 825 g. (7.0 moles) of granulated tin in small portions, the reaction being started after the addition of 30–40 g. of the tin by immersing the flask in a hot-water bath (Note 3). The rest of the tin is added through the condenser at such a rate that the reaction proceeds briskly. It is advisable to carry out this reaction under a hood since hydrogen chloride is apt to escape at the beginning of the reaction. The mixture is finally heated on a steam bath for an hour in order to complete the reaction, and is then filtered hot through glass wool in order to remove unreacted tin.

The filtrate is made up to exactly 2 l. and a 50 cc. sample titrated with sodium hydroxide solution of known concentration (35–40 per cent is a suitable strength). The volume of alkali necessary to produce a slight permanent precipitate is noted (it usually requires 6–8 cc. of 40 per cent alkali). More alkali is run in until the liquid is neutral to litmus paper: this second value

represents the acid combined with tin. To the filtrate in the 5-l. flask is added 1 kilo of cracked ice, and then sufficient alkali to neutralize the free acid as well as 60 per cent of that combined with the tin (about 800 cc. of 40 per cent sodium hydroxide is required). The mixture is diluted, without filtering, to 6 l. and boiled in a 12-l. flask under a reflux condenser in an atmosphere of coal gas (Note 4) for twenty hours. The precipitate is then filtered off and washed very thoroughly with boiling water (2–3 l. of water) and the combined filtrates concentrated to 3 l. This is then rendered slightly acid to litmus with hydrochloric acid, and chilled to 0°, when crystals of phloroglucinol separate. This crop is filtered off; it should weigh 70–80 g. It is then dissolved in 700 cc. of hot water, filtered, and allowed to crystallize at 0°. In this way 65–75 g. (46–53 per cent of the theoretical amount) of almost colorless (Note 5) phloroglucinol dihydrate melting at 217–218° is obtained.

## 2. Notes

1. It is unnecessary to remove the small amount of trinitrotoluene with which the crude trinitrobenzoic acid is contaminated, since it has been found that no trace of the methyl homologue of phloroglucinol is obtained on treating trinitrotoluene in the above manner.

2. An equivalent quantity of 1,3,5-trinitrobenzene may be employed in place of trinitrobenzoic acid with exactly the same result; but as the most convenient method of preparing trinitrobenzene in the laboratory is through trinitrobenzoic acid, nothing is gained by the substitution.

3. In carrying out the reduction, care must be taken that not more than 5 per cent of the tin is added before the reaction starts, otherwise the interaction begins with such violence that the product may be lost. The reaction may be readily checked by immersion of the flask in water. The application of wet towels to the upper half of the flask is often of great assistance to condensation while only slightly checking the reaction itself.

4. Coal gas is recommended as being the most convenient

inert gas in which to carry out the hydrolysis; carbon dioxide or hydrogen should serve equally well.

5. If it is found impossible to obtain a white product by crystallization, purification may be effected by dissolving the phloroglucinol dihydrate in four times its weight of hot boiling water and passing in sulfur dioxide until no further bleaching effect is observed (about half a minute is usually sufficient).

## 3. Methods of Preparation

Phloroglucinol is formed by alkaline fusion of many vegetable products, for instance, maclurin [1] or kino.[2] It is also formed to a small extent by the fusion of phenol with sodium hydroxide,[3] and to a larger extent by fusing resorcinol with sodium hydroxide.[4] It has been produced by fusing 1,3,5-benzenetrisulfonic acid with sodium hydroxide [5] and 3,5-dibromophenol with potassium hydroxide.[6] The best yields, however, are obtained by boiling a dilute solution of triaminobenzene hydrochloride [7] or triaminobenzoic acid hydrochloride [8] with water.

[1] Hlasiwetz and Pfaundler, Ann. **127**, 357 (1863); Benedikt, Ann. **185**, 114 (1877).

[2] Hlasiwetz, Ann. **134**, 122 (1865).

[3] Barth and Schreder, Ber. **12**, 417 (1879).

[4] Barth and Schreder, Ber. **12**, 503 (1879).

[5] Barth and Schreder, Ber. **12**, 422 (1879).

[6] Blau, Monatsh. **7**, 632 (1886).

[7] Weidel and Pollak, Monatsh. **21**, 20 (1900).

[8] Ger. Pat., 102358 [Frdl. V. 156 (1897)].

## XXVII

## PYRROLE

$$CO_2H(CHOH)_4CO_2H + 2NH_4OH \rightarrow CO_2NH_4(CHOH)_4CO_2NH_4 + 2H_2O$$

$$2CO_2NH_4(CHOH)_4CO_2NH_4 \rightarrow 2C_4H_5N + (NH_4)_2CO_3 + 7H_2O + 3CO_2$$

Submitted by S. M. McElvain and K. M. Bolliger.
Checked by H. T. Clarke and E. R. Taylor.

### 1. Procedure

In a 30-cm. evaporating dish or a Pyrex tray are placed 630 g. (3 moles) of mucic acid (Note 1) and 900 cc. of ammonium hydroxide (sp. gr. 0.9); this mixture is rapidly stirred to a smooth paste under the hood. The paste is evaporated to complete dryness on a steam bath, and the resulting ammonium mucate is powdered and mixed with 350 cc. of glycerol (Note 2) in a 5-l. round-bottom Pyrex flask. After standing overnight, the mixture is carefully distilled over a free flame, applying the heat to one side of the flask alone, so that only a portion of the mass is heated to the reaction temperature. The gases, which are evolved with considerable foaming (Note 3), are led away to a gas trap (Org. Syn. **8**, 27) or to the open air, on account of their disagreeable nature. The heating is extended throughout the mass as rapidly as appears possible from the state of the mixture. Distillation is continued until a sample of distillate no longer shows oily drops when treated with solid potassium hydroxide; the total volume of distillate amounts to 900–1000 cc.

The entire distillate is redistilled until no further oil separates in the distillate; the watery layer is then separated and returned to the reaction flask, together with the water remaining in the distilling flask. Two liters more of water is added and about 800 cc. is distilled. The distillate is redistilled until 250–300 cc.

has collected in the receiver. This final distillate, on treatment with solid potash, yields a further 2 g. of oil.

The united oil is rapidly dried with a small quantity of solid potassium hydroxide (Note 4) and distilled. The fraction which boils at 127–131° is collected; this is a colorless liquid which darkens on exposure to light (Note 5). The yield is 75 80 g. (37–40 per cent of the theoretical amount).

## 2. Notes

1. Mucic acid is now manufactured on a large scale by the oxidation of the galactose occurring in certain species of wood.

2. By the use of more glycerol the yield may be slightly increased, but the foaming is very difficult to control. Medicinal mineral oil may be substituted for the glycerol, but the yield is then considerably reduced.

3. Unless the flame is properly adjusted before the foaming becomes very pronounced, there may be difficulty in controlling the distillation. The best method consists in removing the flame from below the flask and allowing it to play on the upper portion of the vessel above the surface of the boiling mixture.

4. When pyrrole is allowed to stand over potassium hydroxide for more than a few hours, combination takes place, lowering the yield.

5. A product of rather better quality, which shows less tendency to darken, may be obtained by finally distilling under reduced pressure. The darkening may also be almost entirely avoided by storing the product in a sealed vessel.

## 3. Methods of Preparation

Pyrrole can be obtained by fractional distillation of bone oil and purification through the potassium derivative.[1] The only synthetic method offering any possibilities involves the thermal decomposition of ammonium mucate, either alone [2] or in presence of glycerol.[3]

[1] Anderson, Ann. **105**, 349 (1858); Weidel and Ciamician, Ber. **13**, 65 (1880); Ciamician and Dennstedt, Ber. **19**, 173 (1886).

[2] Schwanert, Ann. **116**, 278 (1860).

[3] Goldschmidt, Zeit. f. Chem. **1867**, 280; Khotinsky, Ber. **42**, 2506 (1909).

# XXVIII

## o-SULFOBENZOIC ANHYDRIDE

$$C_6H_4\left\langle\begin{matrix}SO_3NH_4\\CO_2H\end{matrix}\right. + SOCl_2 \rightarrow C_6H_4\left\langle\begin{matrix}SO_2\\CO\end{matrix}\right\rangle O + NH_4Cl + SO_2 + HCl$$

Submitted by H. T. CLARKE and E. E. DREGER.
Checked by HENRY GILMAN and J. E. KIRBY.

### 1. Procedure

IN a 2-l. flask fitted with a mechanical stirrer, separatory funnel and an efficient reflux condenser are placed 219 g. (1 mole) of finely powdered acid ammonium *o*-sulfobenzoate (p. 1) and 200 cc. of dry benzene (Note 1). To this is added with stirring 145 g. (1.22 moles) of thionyl chloride (b. p. 76–78°). A tube is connected to the upper end of the reflux condenser which passes into an ice-cooled flask; from this another tube is provided to carry off the hydrogen chloride and sulfur dioxide generated during the reaction (Org. Syn. **8**, 27). The mixture is gently warmed on a steam bath in such a way that gases are evolved fairly briskly (Note 2); continuous stirring is essential. The bulk of the entrained benzene and thionyl chloride is condensed in the ice-cooled receiver; the condensate is returned periodically to the reaction mixture through the separatory funnel. After about fifteen hours' heating, the evolution of gases slackens; an additional 400 cc. of dry benzene is then added and the heating continued until the evolution of gases ceases; this requires about five hours longer.

The hot mixture is then filtered (Note 3) with suction into a 2-l. flask and the solid material, consisting of ammonium chloride, is washed with 100 cc. of hot benzene. This solid is then returned to the 2-l. flask and boiled with stirring for one hour

with 300 cc. of dry benzene; the mixture while hot is then filtered with suction into the same 2-l. flask. The combined filtrates and washings are then distilled until about 300 cc. of benzene has been removed, after which the solution is cooled in an ice bath; this causes the greater part of the sulfobenzoic anhydride to crystallize. The benzene mother liquor is decanted from these crystals and the bulk of the solvent removed by distillation. The flask containing the crystals is attached to a condenser and heated until the solid has completely melted; the adhering solvent is then removed from the liquid by slightly reducing the pressure. The clear residue is poured into a dish and allowed to cool. The product thus obtained melts at 121–123°. The residue from the mother liquor, being as a rule somewhat dark in color, is preferably distilled under reduced pressure (Note 4), the flask being heated in a metal bath. The anhydride distils at 184–186°/18 mm. The second crop may have a slightly lower melting point. The total yield of *o*-sulfobenzoic anhydride, which is of sufficient purity for the preparation of sulfonphthaleins, amounts to 118–121 g. (64–66 per cent of the theoretical amount) (Note 5). In order to convert this into a product melting at 126–127° (Note 4), it is recrystallized from three times its weight of dry benzene.

## 2. Notes

1. The benzene is most satisfactorily dried by distillation, the moist forerun being rejected.

2. The reaction may become so vigorous that it is necessary to interrupt the heating for a short time.

3. The filtration should be carried out under a hood, on account of the presence of some unchanged thionyl chloride.

4. It is stated in the literature that the pure compound melts at 128°. It is very sensitive to moist air, which converts it into the free acid.

5. With larger quantities the yields are significantly increased; the submitters of these directions obtained 74–81 per cent of the theoretical amount with runs of 7.5 moles.

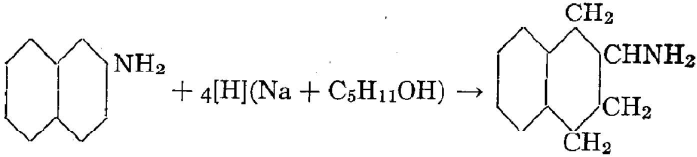
### 3. Methods of Preparation

*o*-Sulfobenzoic anhydride has been prepared from the free acid by heating alone or with phosphorus pentoxide [1] and by treating it with acetyl chloride; [2] from the neutral potassium salt by warming with phosphorus pentachloride; [2] from the acid potassium salt by warming with phosphorus pentachloride [3] or thionyl chloride,[4] and by heating it with phosphorus pentoxide to 400°.[5] The present method is a modification of that of White and Acree [6] who heated the acid ammonium salt with an excess of thionyl chloride and extracted the product with benzene.

[1] Remsen and Dohme, Amer. Chem. *J.* **11**, *343* (1889).
[2] Fahlberg and Barge, Ber. **22**, 757 (1889).
[3] Sohon, Amer. Chem. J. **20**, 258 (1898).
[4] Cobb, Am. Chem. J. **35**, 499 (1906).
[5] Heitman, J. Am. Chem. Soc. **34**, 1594 (1912).
[6] White and Acree, Am. Chem. J. **41**, 1197 (1919).

## XXIX

## *ac*-TETRAHYDRO-β-NAPHTHYLAMINE




Submitted by E. B. H. WASER and H. MÖLLERING.
Checked by ROGER ADAMS and W. W. MOYER.

### 1. Procedure

A 1-l. wide-neck round-bottom flask is set into an iron dish of about 1.3–1.5 l. capacity and the space in between is filled with fine sand so that the flask rests about 1 cm. from the bottom of the dish (Note 1). In the flask is placed 26 g. (1.1 moles) (twice the theoretical amount) of sodium cut into thin slices (Note 2), and the flask is then closed with a tight-fitting cork stopper through which is inserted a separatory funnel (Note 3) and a long, wide, Liebig condenser through the jacket of which is passed downward a rapid current of air (Note 4).

While preparing this set-up a solution of 20 g. (0.14 mole) of β-naphthylamine in 250 cc. of isoamyl alcohol (dried by distilling off a moist forerun) is heated to boiling. The boiling solution is poured in a stream through the separatory funnel into the flask upon the sodium and then washed down with 50 cc. of boiling isoamyl alcohol. A very violent reaction begins immediately which slows up after about five minutes and then must be aided by warming. The flame is so regulated that the reaction mixture is always boiling very vigorously until all of the sodium is dissolved. This generally requires about three

or four hours. If after three hours the sodium is not completely dissolved it is advisable, in order to hasten the reaction, to add 50 cc. more of isoamyl alcohol.

When all of the sodium is completely dissolved, the hot, yellow solution is allowed to cool to about 100° and then poured into 500 cc. of cold water. The mixture is allowed to cool completely with frequent shaking and then the upper isoamyl alcohol layer is separated from the water layer which contains the principal part of the sodium hydroxide.

The reduction is repeated four times with 20 g. of β-naphthylamine so that altogether 100 g. of naphthylamine has been reduced (Note 5). The isoamyl alcohol solutions from all five portions are combined and concentrated hydrochloric acid is added until the solution is just acid to litmus. For this purpose usually about 40–50 cc. is needed (Note 6). The greater part of the isoamyl alcohol is now distilled from a large flask (about 900–1100 cc. is recovered). The distillation is continued until a crust of crystals starts to form, and the residue is then cooled and treated with 200–300 cc. of water and about 300 cc. of 50 per cent potassium hydroxide solution. The base which separates is extracted in the separatory funnel with four 400–500 cc. portions of ether and the ether extracts combined in a flask with a wide neck.

The flask is set in ice water and a rapid stream of carbon dioxide which has previously passed through two wash bottles containing water (Note 7), is passed in. After about a quarter of an hour the liquid begins to become cloudy and soon after there follows a rather rapid separation of the carbonate of the strongly basic alicyclic compound, while the aromatic base does not react and remains in solution. The carbon dioxide is passed in continuously until no more carbonate separates; this requires about four to six hours. The carbonate is filtered by suction on a Büchner funnel and washed with a little dry ether. The filtrate is again treated with carbon dioxide; there is often obtained still more carbonate which is added to the precipitate (Note 8).

For further purification, the almost dry carbonate is dissolved

in 500–600 cc. of 7 per cent acetic acid and the solution is filtered from the dark impurities. The clear, almost colorless solution is decomposed with a large excess of potassium hydroxide (about 200 cc. of a 50 per cent solution), whereupon the alicyclic base separates as a light-brown oil which collects on the surface of the water solution and is extracted as rapidly as possible by shaking three or four times with ether. The ether solution is dried for

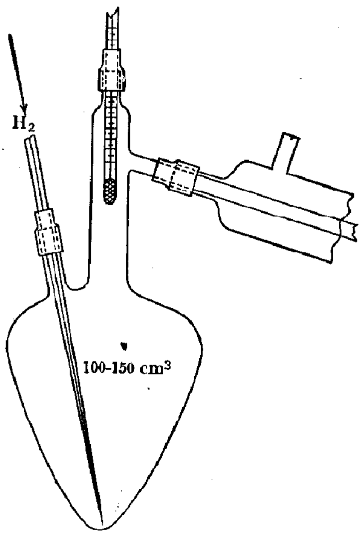



FIG. 1.

at least six hours with about 90–100 g. of potassium hydroxide (Note 9). The distillation of the ether is carried out most conveniently in a specially designed Claisen flask (Org. Syn. 1, 40) of a 100–150 cc. capacity, the ether solution gradually being added to the flask from the separatory funnel.

The base is distilled in a vacuum obtained by a water pump, because it is easily decomposed under ordinary pressure. For this distillation a flask of the form shown in Fig. 1 is recommended for use (Note 10) though not essential.

Since the base is sensitive to oxygen, dry hydrogen is passed through the capillary tube used in the distillation (Note 11). The distillation of the base runs very smoothly and the liquid

distils over from beginning to end almost constantly within a degree.

The yield of pure distilled base, b.p. 118.5°/8 mm., 127.5–128°/12 mm., 140–140.5°/20 mm., amounts to 53–59 g. (51–57 per cent of the theoretical amount). The pure base can be preserved only by sealing it in ampules (containing as little air as possible) immediately after distillation. The *ac.*-tetrahydro-β-naphthylamine is a colorless, water-clear liquid which shows no fluorescence (Note 12), and possesses a strong odor similar to piperidine. In the air the base soon turns brown, rapidly absorbs carbon dioxide and changes to the carbonate.

The hydrochloride of the *ac.*-tetrahydro-β-naphthylamine can be obtained readily by neutralizing a dry ether solution of the base with an ether solution of hydrogen chloride. It crystallizes from water in large plates which melt at 237°.

## 2. Notes

1. In place of the sand bath it is possible to use an ordinary wire gauze or a Babo's air bath but the danger of a fire due to a sudden breaking of the flask during the very violent reaction at the beginning is considerably greater. The experiment is best carried out using a sand bath. The hands should be protected with gloves and the eyes with glasses.

2. After many experiments this amount of sodium was found to be the optimum. By the use of smaller quantities of sodium and β-naphthylamine the yield drops; with larger amounts the danger of breaking the glass flask increases. It is probably possible to use copper flasks but it is then impossible to see how the reaction is running.

3. The stopcock of the separatory funnel must have as wide a hole as possible so that the isoamyl alcohol can enter in a rapid stream.

4. If a water condenser is used the condensation is much more efficient but the danger of breaking is then much greater. A brass inner tube in place of a glass one is desirable. If the condenser tube is too narrow, there is danger that the violently

boiling isoamyl alcohol will be thrown out at the beginning of the reaction because it cannot flow back.

5. By working up less than 100 g. of β-naphthylamine the yield decreases rather rapidly on account of the various possibilities for loss in the later operations.

6. An excess of acid does no harm but makes the recovery of the isoamyl alcohol more difficult.

7. If an efficient reflux condenser is attached to the flask the major part of the ether can be recovered. It is necessary to be sure that the carbon dioxide is actually moist because otherwise the carbonate will not form at all or only very slowly.

8. The ether filtrates contain dihydronaphthalene and *ar*-tetrahydro-β-naphthylamine.

9. Since the free base reacts very strongly alkaline and also is sensitive, it is not possible to allow it to remain long in the air or loss will occur due to carbonate formation and oxidation.

10. The suggested flask has the following advantages over other forms:

(*a*) The chance for contaminating the boiling base with rubber is reduced to a minimum; the capillary and thermometer are attached to the distillation flask by means of small rubber tubing.

(*b*) The loss due to the substance which remains on the walls of the flask is reduced to a minimum as compared to other flasks.

(*c*) The substances can, with the help of the capillary be distilled over to the last drop, which is not possible in a round flask.

11. This apparatus has also proved itself very useful for the distillation of other substances sensitive to oxygen.

12. Fluorescence arises from aromatic by-products which, however, can be entirely separated by careful work. Pure *ac*-tetrahydro-β-naphthylamine gives no color with diazobenzene sulfonic acid.

13. Of special interest is the extremely powerful physiological action of the tetrahydro base and its salts,[1] which makes

[1] Bamberger and Filehne, Ber. **22**, 777 (1889); Stern, Virchows Archiv., **115**, 14 (1889); **117**, 418 (1889); Pick, Arch. f. exp. Pathologie u. Pharmakologie

it advisable to handle it carefully. The action can be called a symptom-complex to which Barger has assigned the name, "sympathomimetic," and it consists in a maximum dilation of the pupils (mydriasis), in a marked increase in the arterial blood pressure and in an increase in the rapidity of breathing.

### 3. Methods of Preparation

Up to the present the only method used for the reduction of β-naphthylamine for obtaining the tetrahydro base has been with sodium and alcohol. This method was first described by Bamberger and Müller.[2] It is possible to substitute ethyl alcohol for amyl alcohol but the yield is distinctly lower. The base has been resolved into its optically active components.[3]

*(A. Path.)* **42**, *399 (1899); Weichowsk, A. Path.* **52**, *417 (1905); Jonescu, A. Path.* **60**, 345 (1909); Cloetta and Waser, A. Path. **73**, 398, 436 (1913); **75**, 406 (1914); **77**, 16 (1914); **79**, 30 (1915); **98**, 198 (1923); Sacharof, Zeitschr. f. exp. Pathologie u. Therapie, 7, 225 (1909).

[2] Bamberger and Müller, Ber. **21**, 847 (1888); see also Bamberger and Kitschelt, Ber. **23**, 876 (1890); Waser, Ber. **49**, 1202 (1916); Cloetta and Waser, A. Path. **73**, 398 (1913); **98**, 198 (1923).

[3] Pope and Harvey, J. Chem. Soc. **79**, 74 (1901); Waser, A. Path. **73**, 401 (1913).

# LATER REFERENCES TO PREPARATIONS IN PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been recently described. The numbers in parentheses following the name of a compound refer to the volume and page of Organic Syntheses.)

**Acetal** (3, 1):

(*a*) From ethyl alcohol and paraldehyde, using *p*-toluenesulfonic acid or hydrogen chloride as catalyst. BEDUWÉ, Bull. soc. chim. Belg. **34**, 41 (1925).

(*b*) By the interaction of ethyl alcohol and metaldehyde in presence of calcium chloride, a trace of hydrogen chloride, and high-boiling (200–300°) petroleum. The acetal is removed from the reaction mixture by virtue of its solubility in the petroleum. The yields are stated to reach 90 per cent of the theoretical amount. FOUQUE and CABANAC, Bull. soc. chim. **39**, 1184 (1926).

(*c*) Calcium chloride is stated to be a better catalyst than ferric chloride for the formation of diethyl acetal, though the reverse is the case for dimethyl acetal. ADAMS and ADKINS, J. Amer. Chem. Soc. **47**, 1358 (1925).

**Acetamide** (3, 3):

By passing the vapor of methyl alcohol and hydrogen cyanide over catalysts at high temperatures. SMITH and SMITH, can. pat. 274,065 (1927).

**Adipic acid** (5, 9):

Isolation from cellulose waste liquors. MELANDER and WALLIN, Swed. pat. 62,919 [C. A. **21**, 4069(1927)].

***l*-Arabinose** (8, 18):

Same procedure as described in Org. Syn. ANDERSON and SANDS, J. Am. Chem. Soc. **48**, 3172 (1926).

**Butyl Butyrate** (**5**, 23):

By oxidizing butyl alcohol with sodium chlorate and dilute sulfuric acid, using vanadium pentoxide as a catalyst. MILAS, J. Amer. Chem. Soc. **50**, 493 (1928).

This reaction may lead to violent explosions if the sodium chlorate be replaced by potassium perchlorate and if the temperature be not carefully controlled. WAGNER, J. Amer. Chem. Soc. **50**, 1233 (1928).

*p*-**Cresol** (**3**, 37):

Traces of isomeric cresols may be removed by treatment with quinone chloroimide. GIBBS, J. Amer. Chem. Soc. **49**, 839 (1927).

**Cyclopentanone** (**5**, 37):

Occurrence in lignite distillation products. VORLÄNDER and GÖRNANDT, Z. Angew Chem. **39**, 1116 (1926).

**Ethyl cyanoacetate** (**3**, 53; **8**, 74):

The W. A. NOYES method of preparation [J. Am. Chem. Soc. **26**, 1545 (1904)] from ethyl chloroacetate and potassium cyanide in methyl alcoholic solution gives a mixture of methyl and ethyl esters. URUSHIBANA, Bull. Chem. Soc. Japan **2**, 143 (1927) [C. A. **21**, 2879 (1927)].

**2-Furancarboxylic acid** (**6**, 44):

Subsequent to the Cannizzaro reaction, sufficient sulfuric acid is added to liberate substantially all of the pyromucic acid and to cause resinification *in situ* of the 2-furylcarbinol when the mixture is heated. TRICKEY and MINER, U. S. pat. 1,665,236 [C. A. **22**, 1783 (1928)].

**Furfural** (**1**, 49):

From oat hulls. BRONLEE, Ind. Eng. Chem. **18**, 422 (1927).

*d*-**Glutamic acid** (**5**, 63):

Recovery from molasses waste. TRESSLER, Can. pat. 268,728. [C. A. **21**, 2395 (1927).]

**Glycerol α-monochlorhydrin** (**2**, 33):

By heating epichlorhydrin with water in the presence of sulfuric acid as a catalyst. FOURNEAU and RIBAS Y MARQUÈS, Bull. soc. chim. (4) **39**, 700 (1926); see also BOESEKEN and HERMANS, Rec. trav. chim. **42**, 1106 (1923).

**Hydroxylamine salts** (**3**, 61):

By electrolytic reduction of sodium nitrate in 65 per cent sulfuric acid. PONZIO and PICHETTO, Chem. Abstr. **19**, 239 (1925).

**Mandelic acid** (**6**, 58):

From phenylglyoxal by means of biocatalysts. [MAYER, Biochem. Z. **174**, 420 (1926)] and by enzyme action [KUHN and HECKSCHER, Z. physiol. Chem. **160**, 116 (1926)].

**Mercury Di-*p*-Tolyl** (**3**, 65):

By treating *p*-tolyl mercuric chloride with copper in pyridine. This appears to be a general method. HEIN and WAGLER, Ber. **58**, 1499 (1925).

***m*-Nitro Chlorobenzene** (**3**, 79):

From *m*-nitroaniline by the Sandmeyer reaction. KOHMAN, J. Phys. Chem. **29**, 1052 (1925).

**Nitromethane** (**3**, 83):

By heating methyl *p*-toluenesulfonate with sodium nitrite. RODIONOW, ALEXEIEFF and CARCARRAS, Bull. Soc. Chim. (4) **39**, 324 (1926).

***m*-Nitrophenol** (**3**, 87):

Formed in 2–3 per cent yield (together with ortho and para derivatives) by nitrating phenol in glacial acetic acid. ARNALL, J. Chem. Soc. **125**, 811 (1924).

**Nitrourea** (**5**, 85):

New method of purification by recrystallization from alcohol. WILLSTÄTTER and PFANNENSTIEL, Ber. **59B**, 1870 (1926).

**Quinizarin** (**6**, 78):

Differs from the general procedure described in Org. Syn. by starting with a mixture of *o*- and *p*-chlorophenol and heating above 200°. DODD, SPRENT and United Alkali Co., Ltd., Brit. pat. 245,584 (1924). [C. A. **21**, 249 (1927)].

**Styrene** (**8**, 84):

Separated from carburetted water gas drip oil by fractionation. BROWN, U. S. pat. 1,640,975 [C. A. **21**, 3449 (1927)].

# SUBJECT INDEX

*(This Index Comprises Material from all Volumes of this Series)*

(Names of compounds in small capital letters indicate substances for which directions are given, the numbers in bold face type refer to volumes of Organic Syntheses, numbers in italics refer to pages in those volumes on which preparative directions are given, and numbers in Arabic refer to pages on which the compounds or subjects are mentioned in connection with other preparations. For example: ACETOACETIC ESTER, **4**, 45; **6**, *36* indicates that acetoacetic ester is mentioned in volume 4 on page 45 and that directions for its preparation are given in detail in volume 6 on page 36; Acetophenone, **2**, 1 indicates that this substance is mentioned in volume 2 on page 1 but that no directions for its preparation are given in this series.)

## A

B

Q



R

## S

# ORGANIC SYNTHESES

## AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS



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# PREFACE TO VOLUME X

The present volume forms the first annual number in the second decade of this series. A revised collection of the material presented in the first nine volumes is in preparation, so that no attempt has been made to refer to these volumes in the Index. Otherwise, no departure has been made from the general plan adopted in recent numbers, beyond the inclusion of a rather greater proportion of organic preparations of a biochemical rather than a strictly synthetic character.

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# ORGANIC SYNTHESES

## I

## ACETOL

$$HCO_2C_2H_5 + KOH \rightarrow HCO_2K + C_2H_5OH$$
$$CH_3COCH_2Br + HCO_2K \rightarrow CH_3COCH_2OCHO + KBr$$
$$CH_3COCH_2OCHO + CH_3OH \rightarrow CH_3COCH_2OH + HCO_2CH_3$$

Submitted by P. A. LEVENE and A. WALTI.
Checked by FRANK C. WHITMORE and J. PAULINE HOLLINGSHEAD.

### 1. Procedure

IN a 3-l. round-bottom flask fitted with a 75-cm. Liebig condenser is placed 210 g. of potassium hydroxide (purified with alcohol) dissolved in 1500 cc. of anhydrous methyl alcohol. The solution is cooled to below 50° (Note 1), 300 g. of purified ethyl formate is added and the mixture is refluxed for two hours (Notes 2 and 3).

Then 410 g. (257 cc., 3 moles) of bromoacetone (page 12) is added and the mixture is refluxed for sixteen hours on a water bath at 95–97°. At the end of the operation the solution is cooled to 0° in an ice-salt bath. The potassium bromide which settles out is filtered off on a cooled suction filter and the filtrate is fractionated.

The fraction boiling at 23–35°/12 mm. is discarded, as it contains very little acetol. The main fraction distils at 35–47°/12 mm. and weighs 160 g. This is refractionated. The fraction boiling at 40–43°/12 mm. weighs 120–130 g. (54–58 per cent of the theoretical amount) (Note 4).

## 2. Notes

1. It is necessary to cool the mixture below 50° to prevent the ethyl formate from boiling out.

2. Technical ethyl formate was purified by washing with 3 per cent sodium carbonate solution, then with cold water, drying over anhydrous sodium sulfate, filtering, and fractionating. It is very important that all the materials used in the synthesis of acetol be anhydrous, as otherwise condensation products are formed.

3. If commercial potassium formate is used it should be dried under reduced pressure at 80°. One and one-half to two moles should be used per mole of the bromo compound.

4. Acetol polymerizes very readily on standing but remains unchanged when dissolved in an equal volume of methyl alcohol.

## 3. Methods of Preparation

Nef prepared acetol in several ways, the more important of which depended upon the reaction between bromoacetone and potassium or sodium formate or acetate, and the subsequent hydrolysis of the ester by methyl alcohol.[1,2] Acetol is also formed, together with pyruvic acid, by the direct oxidation of acetone by Baeyer and Villiger's acetone-peroxide reagent.[3]

[1] Nef, Ann. **335**, 260 (1904).
[2] Nef, Ann. **335**, 247 (1904).
[3] Pastureau, Bull. soc. chim. (4) **5**, 227 (1909).

## $n$-AMYL BENZENE

$$C_6H_5CH_2Cl + Mg \rightarrow C_6H_5CH_2MgCl$$

$$C_6H_5CH_2MgCl + 2p\text{-}CH_3C_6H_4SO_3C_4H_9 \rightarrow$$
$$C_6H_5(CH_2)_4CH_3 + C_4H_9Cl + (p\text{-}CH_3C_6H_4SO_3)_2Mg$$

Submitted by HENRY GILMAN and J. ROBINSON.
Checked by C. S. MARVEL and S. S. ROSSANDER.

### 1. Procedure

ONE mole of benzylmagnesium chloride is prepared in a 2-l. three-neck round-bottom flask from 24.3 g. (1 mole) of magnesium turnings, 126.5 g. (1 mole) of benzyl chloride and 500 cc. of anhydrous ether, according to the directions given in Org. Syn. **4**, 59. Stirring should be commenced with the first addition of the benzyl chloride. The time of addition of the benzyl chloride in this preparation is about two hours. When all has been added, the mixture is gently boiled for about fifteen minutes (Note 1).

The solution is cooled with running water, and 456 g. (2 moles) of $n$-butyl $p$-toluenesulfonate (Org. Syn. **9**, 28) dissolved in about twice its volume of anhydrous ether is then added slowly with stirring through the separatory funnel at such a rate that the ether just boils. The time required for the addition is about two hours. A white solid soon forms and the mixture assumes the consistency of a thick cream. Stirring is continued, without cooling, for about two hours, and the mixture is hydrolyzed by pouring onto crushed ice to which is then added about 125 cc. of concentrated hydrochloric acid (Note 2).

The ether layer is separated and combined with a 200-cc. ether extract of the aqueous layer. The combined ether solution is washed once with about 100 cc. of water and then dried by shaking for a few minutes with about 10 g. of anhydrous

potassium carbonate. After filtration, the ether is distilled on a water bath. When practically all of the ether has distilled, about 5 g. of sodium, freshly cut and in thin slices, is added and the mixture is boiled for about two hours (Note 3). The solution is decanted and then distilled, using an efficient fractionating column. The fraction boiling at 190–210° is collected. This on redistillation yields 74–88 g. (50–60 per cent of the theoretical amount) of *n*-amyl benzene boiling at 198–202° (Note 4).

## 2. Notes

1. It has recently been shown[1] that benzyl magnesium chloride can be prepared without essential impairment of yield by the rapid addition of benzyl chloride to magnesium in ether.

2. The hydrolysis is preferably carried out in a 5-l. Erlenmeyer flask. The magnesium *p* toluenesulfonate is sparingly soluble in hydrochloric acid, and complete solution is brought about by the subsequent addition of about 2 l. of water.

3. Refluxing with sodium helps to remove the small amount of benzyl alcohol formed by the atmospheric oxidation of benzylmagnesium chloride.

4. The major part of the *n*-amyl benzene distils at 199–201°. A careful fractionation of the distillate that comes over around 75° yields 24 g. (26 per cent of the theoretical amount) of *n*-butyl chloride boiling at 76–80°.

## 3. Methods of Preparation

The method described here has been adapted from the directions of Gilman and Heck,[2] and Rossander and Marvel.[3] *n*-Amyl benzene has also been prepared by the action of sodium on a mixture of benzyl and *n*-butyl bromides,[4] and by heating *n*-butyl phenyl ketone and formic acid with copper at 300°.[5]

[1] Gilman, Zoellner and Dickey, J. Am. Chem. Soc. **51**, 1583 (1929).
[2] Gilman and Heck, J. Am. Chem. Soc. **50**, 2223 (1928).
[3] Rossander and Marvel, J. Am. Chem. Soc. **50**, 1491 (1928).
[4] Schramm, Ann. **218**, 388 (1883).
[5] Mailhe and de Godon, Bull. soc. chim. (4) **21**, 62 (1917).

III

## BENZENESULFOCHLORIDE

$$C_6H_6 + 2ClSO_3H \rightarrow C_6H_5SO_2Cl + H_2SO_4 + HCl$$

Submitted by H. T. Clarke, G. S. Babcock, and T. F. Murray.
Checked by Frank C. Whitmore and A. M. Griswold.

### 1. Procedure

In a 5-l. flask, fitted with stirrer, dropping funnel, exit tube, and thermometer, is placed 3500 g. (30 moles) of chlorosulfonic acid (Note 1), and to it is slowly added, with continuous stirring, 780 g. (10 moles) of benzene (Note 2), keeping the temperature between 20° and 25° by means of cold water. The hydrogen chloride which is evolved is led to a hood or absorbed in water. The addition requires two to three hours; when this is complete, the mixture is stirred for an hour, and poured onto 6–7 kg. of crushed ice (Note 3). One liter of carbon tetrachloride is then added, the oil is separated as soon as possible (Note 4), and the watery layer is shaken with 500 cc. of carbon tetrachloride. The combined oil is washed with dilute sodium carbonate, and the bulk of the carbon tetrachloride is distilled under atmospheric pressure (Note 5); the pressure is then reduced (Note 6) and the benzenesulfochloride collected at 113–115°/10 mm. (118–120°/15 mm.). The yield is 1320–1360 g. (75–77 per cent of the theoretical amount) of a colorless liquid which on cooling sets to a crystalline solid melting at 13–14°.

A small amount (50–100 g.) of a higher boiling material remains in the flask. This is mainly diphenyl sulfone, which may be isolated by distillation under reduced pressure (b.p. 225°/10 mm.) and recrystallization from methyl alcohol. It forms colorless crystals which melt at 128°.

## 2. Notes

1. If less than 50 per cent excess of chlorosulfonic acid is taken, the yield of diphenyl sulfone increases at the expense of the sulfochloride.

2. A good commercial grade of benzene, boiling over a 1° range, is satisfactory. The benzene must be added to the acid (not vice versa); otherwise, a larger proportion of sulfone is formed.

3. The benzenesulfochloride separates at first as a crystalline solid which melts as the temperature rises. It was found impracticable to filter off this solid, owing to its tendency to melt on the funnel.

4. The sulfochloride should be removed from the water as soon as possible; otherwise, the yield falls, owing to hydrolysis. In one run in which the mixture was allowed to stand overnight before separating, only 1220 g. (69 per cent) was obtained. If difficulty is experienced in the separation, owing to the presence of suspended solid matter, the oil may first be filtered with suction through a hardened paper or felt cloth. As a rule, it is merely necessary to filter the sludgy layer lying between the oil and the water.

5. The carbon tetrachloride vapor carries with it any moisture that may be present. If this were not removed at a relatively low temperature, hydrolysis of the chloride would take place, with the formation of sulfonic acid which would promote decomposition of the sulfochloride during its distillation.

6. The pressure should be reduced gradually, and the first runnings, mainly carbon tetrachloride, collected separately.

## 3. Methods of Preparation

The preparation of benzenesulfochloride from sodium benzenesulfonate with phosphorus pentachloride or phosphorus oxychloride has already been described in a previous article in this series,[1] in which a bibliography of the literature is to be

[1] Adams and Marvel, Org. Syn. **1**, 21 (1921).

found. To this bibliography should be added the following references: by the action of phosphorus pentachloride on diphenyl sulfone;[2] by the action of chlorine on benzenesulfinic acid;[3] by the action of phosphorus pentachloride on benzenesulfonic acid;[4] from diphenyl sulfoxide and chlorine;[5] by the action of sulfuryl chloride on benzene in the presence of anhydrous aluminium chloride;[6] by the action of benzene on chlorosulfonic acid, followed by the addition of water.[7] The present process is based on those of Pummerer[8] and of Ullmann.[9]

[2] Gerhardt and Chancel, Jahresb. **1852**, 433; Otto, Ann. **136**, 157 (1865).

[3] Otto, Ann. **145**, 321 (1868).

[4] Mohrmann, Ann. **410**, 379 (1915); Rosenmund and Struck, Ber. **54**, 439 (1921).

[5] Boeseken and Waterman, Rec. trav. chim. **29**, 326 (1910).

[6] Boeseken, Rec. trav. chim. **30**, 382 (1911).

[7] Saccharinfabrik A.G., Ger. pat. 224,386, Frdl. **10**, 114 (1913).

[8] Pummerer, Ber. **42**, 1802, 2274 (1909).

[9] Ullmann, Ber. **42**, 2057 (1909).

## IV

## BENZOPHENONEOXIME

$$(C_6H_5)_2CO + H_2NOH \cdot HCl + NaOH \rightarrow (C_6H_5)_2C{=}NOH + 2H_2O + NaCl$$

Submitted by ARTHUR LACHMAN.
Checked by C. R. NOLLER.

### 1. Procedure

A MIXTURE of 100 g. (0.55 mole) of benzophenone, 60 g. (0.86 mole) of hydroxylamine hydrochloride, 200 cc. of 95 per cent ethyl alcohol, and 40 cc. of water is placed in a 2-l. round-bottom flask. To this is added in portions, with shaking, 110 g. (2.76 moles) of powdered sodium hydroxide. If the reaction becomes too vigorous, cooling with tap water may be necessary. After all the sodium hydroxide has been added, the flask is connected to a reflux condenser, heated to boiling, and refluxed for five minutes. After cooling, the contents are poured into a solution of 300 cc. of concentrated hydrochloric acid in 2 l. of water. The precipitate is filtered with suction, thoroughly washed with water, and dried (Note 1). The yield is 106–107 g. (98–99 per cent of the theoretical amount) of a product melting at 141–142°. On crystallizing 20 g. from 80 cc. of methyl alcohol, there is obtained 13 g. of crystalline material of the same melting point (Note 2).

### 2. Notes

1. This crude material dried over night at about 40° is practically pure and if used at once is satisfactory for the preparation of diphenylmethane imine hydrochloride (p. 28).

2. In the presence of oxygen and traces of moisture, benzo-

phenoneoxime is gradually converted into a mixture of benzophenone and nitric acid.[1] A good method of preserving this substance is to dry it in a vacuum desiccator, fill the desiccator with pure carbon dioxide, re-evacuate, and fill again with carbon dioxide. The preparation may then be transferred to a bottle, also filled with carbon dioxide, and sealed against access of air.

## 3. Methods of Preparation

Benzophenoneoxime has been prepared in quantity by treating an aqueous alcoholic mixture of benzophenone and hydroxylamine hydrochloride with hydrochloric acid,[2] with sodium carbonate,[3] with alcoholic potassium hydroxide,[4] or with aqueous sodium hydroxide.[5] It has also been obtained by treating bisnitrosylbenzohydryl with alcoholic potassium hydroxide,[6] and by the oxidation of $\alpha$-aminodiphenylmethane with magnesium persulfate solution.[7]

[1] Hollemann, Rec. trav. chim. **13**, 429 (1894); Lachman, J. Am. Chem. Soc. **46**, 1478 (1924).

[2] Beckmann, Ber. **19**, 989 (1886).

[3] Janny, Ber. **15**, 2782 (1882).

[4] Derick and Bowmann, J. Am. Chem. Soc. **35**, 1287 (1913).

[5] Lachman, J. Am. Chem. Soc. **46**, 1477 (1924); **47**, 260 (1925).

[6] Behrend and Platner, Ann. **278**, 369 (1894).

[7] Bamberger and Seligman, Ber. **36**, 704 (1903).

V

## BROMOACETONE

$$CH_3COCH_3+Br_2 \rightarrow CH_3COCH_2Br+HBr$$

Submitted by P. A. LEVENE.
Checked by FRANK C. WHITMORE and J. PAULINE HOLLINGSHEAD.

### 1. Procedure

A 5-l. three-neck round-bottom flask is provided with an efficient mechanical stirrer, a 48-cm. Allihn reflux condenser, a thermometer, and a 500-cc. separatory funnel, the stem of which reaches nearly to the bottom of the flask (Note 1).

Through the separatory funnel are introduced 1600 cc. of water, 500 cc. of C. P. acetone, and 372 cc. of glacial acetic acid. The stirrer is started and the temperature of the water bath is raised to 70–80°, so that the mixture in the flask is at about 65° (Note 2). Then 354 cc. (7.3 moles) of bromine is carefully added through the separatory funnel. The addition is so regulated as to prevent the accumulation of unreacted bromine (Note 3). The addition requires one to two hours. As a rule the solution is decolorized in about twenty minutes after the bromine has been added. When the solution is decolorized, it is diluted with 800 cc. of cold water, cooled to 10°, made neutral to Congo Red with about 1000 g. of solid anhydrous sodium carbonate, and the oil which separates is collected in a separatory funnel and dried with 80 g. of anhydrous calcium chloride. After drying, the oil is fractionated and the fraction boiling at 38–48°/13 mm. is collected. The yield is 470–480 g. (47–48 per cent of the theoretical amount). It may be used without further purification for the preparation of acetol (p. 1), but if a purer product is desired, the above product is refractionated

and the fraction boiling at 40–42°/13 mm. is collected. The yield is 400–410 g. (40–41 per cent of the theoretical amount).

The higher boiling fraction contains a mixture of isomeric dibromoacetones.

## 2. Notes

1. The apparatus should be set up with the flask in a large container (such as a 14-qt. galvanized pail) to be used as a water bath, and under a well-ventilated hood, as both the bromine and bromoacetone are powerful irritants to the skin and mucous membranes.

2. It is necessary that the reaction mixture be warmed to this temperature to insure a smooth reaction.

3. It is not advisable to have too great an excess of bromine present at any time, as it sometimes reacts suddenly with great violence.

## 3. Methods of Preparation

Bromoacetone may be prepared by allowing bromine and acetone to stand with ten times the volume of water, and steam distilling the resulting oil.[1] It may also be prepared by conducting 138 parts of bromine into 100 parts of cold acetone by means of a current of air.[2] Scholl and Matthaiopoulos prepared bromoacetone by introducing 1 part of bromine into 4 parts of acetone in which 1 part of marble was suspended, and gradually pouring into the mixture 2.5 parts of water.[3] Bromoacetone was prepared by Richards by the electrolysis of a mixture of acetone and hydrobromic acid.[4] It has also been prepared by allowing a dilute methyl alcohol solution of chloroacetone and potassium bromide to stand a long time.[5] The method here used is essentially that of Nef.[6]

[1] Sokolowsky, Ber. **9**, 1687 (1876).
[2] Emmerling and Wagner, Ann. **204**, 29 (1880).
[3] Scholl and Matthaiopoulos, Ber. **29**, 1555 (1896).
[4] Richards, Compt. rend. **133**, 879 (1901).
[5] Brendler and Tafel, Ber. **31**, 2683 (1898).
[6] Nef, Ann. **335**, 259 (1904).

# VI

## α-BROMONAPHTHALENE

$$C_{10}H_8 + Br_2 \rightarrow \alpha\text{-}C_{10}H_7Br + HBr$$

Submitted by H. T. Clarke and M. R. Brethen.
Checked by J. B. Conant and G. W. Wheland.

### 1. Procedure

In a 1-l. flask are placed 512 g. (4 moles) of naphthalene and 275 g. (170 cc.) of carbon tetrachloride. The flask is equipped with a stirrer, an efficient reflux condenser, and a dropping funnel, the stem of which extends below the level of the liquid. From the top of the reflux condenser a tube leads to a water trap similar to that described in Org. Syn. **8**, 28. The mixture is warmed on the steam bath to gentle boiling, and 707 g. (220 cc., 4.4 moles) of bromine is run in at such a rate that practically none of it is carried over with the hydrogen bromide into the trap. This requires from twelve to fifteen hours, during which time the mixture is gently warmed on the steam bath, with continual stirring, until the evolution of hydrogen bromide ceases (about six hours). The mixture is now distilled from the steam bath under slightly reduced pressure (using a condenser) until free of carbon tetrachloride; the residue is mixed with 20–30 g. of powdered or granulated sodium hydroxide and stirred at 90–100° for four hours (Note 1). The liquid is transferred to a flask for fractional distillation and distilled under reduced pressure. The forerun contains a considerable proportion of unchanged naphthalene, the bulk of which is removed by chilling and filtering with suction; the main fraction, consisting of bromonaphthalene, passes over at 160–165°/15 mm., and a high-boiling fraction (175–185°/15 mm.), consisting of dibromo-

naphthalene, is collected. The intermediate fractions and the filtrates from the foreruns are systematically redistilled; in this way 600–620 g. of colorless α-bromonaphthalene (72–75 per cent of the theoretical amount) and about 30 g. of a mixture of dibromonaphthalenes (m.p., about 60°) are obtained.

## 2. Notes

1. If this treatment with sodium hydroxide is omitted, the final product contains impurities which gradually give off hydrogen bromide.

## 3. Methods of Preparation

The above method has been found to be more convenient and to give considerably better yields than that described previously.[1] Bromination of naphthalene in carbon tetrachloride solution has also recently been described by Blicke.[2]

[1] Clarke and Schram, Org. Syn. **1**, 35.
[2] Blicke, J. Am. Chem. Soc. **49**, 2846 (1927).

# VII

## CASEIN

Submitted by E. J. Cohn and J. L. Hendry.
Checked by H. T. Clarke and W. M. Kennan.

### 1. Procedure

To one liter of milk, from which the cream has been largely separated (Note 1), 0.05 M hydrochloric acid is slowly added with stirring through a capillary tube extending to the bottom of the beaker. The addition is continued until the solution attains a *p*H of 4.6 (Note 2). The end-point is determined by withdrawing 5-cc. samples, diluting to 50 cc., adding methyl red, and matching against a buffered series (Note 3). Approximately 1000 cc. of acid is required; the separation of the casein is practically complete at this point. Three liters of water is then added, stirring is discontinued, and the flocculent precipitate of casein is allowed to settle in the refrigerator for twelve to twenty-four hours. The clear supernatant liquid which contains soluble proteins and salts is removed as completely as possible by siphoning; the precipitate is collected on a suction funnel and washed with cold distilled water until the washings are free of calcium (give no precipitate with ammonium oxalate).

The casein, which is contaminated with calcium phosphate and fats, is filtered off to as small a volume as possible (about 500 cc.) and transferred to a 2-l. beaker. It is then treated with 0.1 M sodium hydroxide, the alkali being added slowly and with stirring through a capillary extending to the bottom of the beaker (Note 4). The addition of alkali is continued until the *p*H of the mixture reaches 6.3 (Note 5); 100–150 cc. of the alkali is required. The end-point is determined by matching against

a buffered series (Note 6), employing dibromo-*o*-cresolsulfonphthalein (" bromocresol purple "). At this *p*H the casein is completely in solution in the form of its sodium salt; fats, calcium phosphate and any calcium caseinate remain undissolved. Care must be taken not to add more alkali than is necessary to bring the *p*H to the above point (Note 4). The milky solution is filtered through a thick layer (10–15 mm.) of filter paper pulp tightly packed upon a suction funnel. The filtrate may be slightly opalescent; if it is less clear it is again filtered through a fresh layer of pulp.

The filtrate is brought to a *p*H of 4.6 with 0.05 M hydrochloric acid just as in the original precipitation, the necessary amount of acid being determined by titration of an aliquot portion, diluted five-fold, with 0.01 M hydrochloric acid; 220–250 cc. of 0.05 M acid is required. As the reprecipitation progresses, the rate at which the acid is added is decreased in order to prevent precipitation at the tip of the capillary tube; vigorous mechanical stirring is, of course, essential. When the acidification is complete, 5 l. of cold distilled water is added and the flocculent precipitate allowed to settle in the refrigerator. After siphoning off the clear supernatant liquid, the casein is collected on a suction funnel, using hardened paper, washed with cold distilled water until free of chloride, sucked as dry as possible and dried over calcium chloride in a vacuum desiccator. The yield is 23–29 g. of a colorless coherent product which may readily be pulverized in a mortar.

## 2. Notes

1. The cream is satisfactorily removed by allowing the milk to stand in a refrigerator over night and siphoning off the lower layer.

2. Casein exists in milk in the form of a calcium derivative; *p*H 4.6 is the isoelectric point of free casein, which is soluble to the extent of only 0.11 g. per liter.[1]

[1] Cohn, J. Gen. Physiol. **4**, 697 (1922).

3. Buffers for this range may be made up as follows:

| 0.1 M Acetic Acid | 0.1 M Sodium Acetate | pH |
|---|---|---|
| 7.35 cc. | 2.65 cc. | 4.2 |
| 6.3 | 3.7 | 4.4 |
| 5.1 | 4.9 | 4.6 |
| 4.0 | 6.0 | 4.8 |
| 2.95 | 7.05 | 5.0 |

4. It is important to avoid a local excess of alkali, which would tend to denature the casein.[2]

5. At this pH sodium caseinate is largely dissolved, whereas calcium caseinate is largely undissolved.[3]

6. The buffer series may conveniently be prepared as follows:

| Disodium Phosphate (M/15) | Monopotassium Phosphate (M/15) | pH |
|---|---|---|
| 0.78 cc. | 9.22 cc. | 5.8 |
| 1.2 | 8.8 | 6.0 |
| 1.85 | 8.15 | 6.2 |
| 2.65 | 7.35 | 6.4 |
| 3.75 | 6.25 | 6.6 |
| 5.0 | 5.0 | 6.8 |

### 3. Methods of Preparation

The precipitation of casein in its uncombined form by the addition to milk of one or another acid, forms the basis of all methods of preparation. These differ widely, however, in the subsequent purification. In the method of Hammarsten,[4] just *enough alkali is added to dissolve this casein completely.* The alkalinity reached in this process somewhat modifies its physical properties but probably not its composition. In the method of Van Slyke and Bosworth [5] the last trace of calcium is removed by adding oxalate to an ammoniacal solution of the casein, but

[2] Cohn and Hendry, J. Gen. Physiol. **5**, 521 (1923).

[3] Loeb, J. Gen. Physiol. **3**, 547 (1920–21).

[4] Hammarsten, Textbook of Physiological Chemistry, translation of 7th Edition, 619 (John Wiley, 1911).

[5] Van Slyke and Bosworth, J. Biol. Chem. **14**, 211 (1913).

this procedure was shown to be unnecessary by Van Slyke and Baker.[6]

The present process is based in large part upon that of Van Slyke and Baker, the modifications depending upon the observation that casein forms far more soluble compounds with univalent than with bivalent bases at neutral reactions.

[6] Van Slyke and Baker, J. Biol. Chem. **35**, 127 (1918).

# VIII

## o-CHLOROBENZOIC ACID

$$ClC_6H_4CH_3 + 2KMnO_4 \rightarrow ClC_6H_4COOK + 2MnO_2 + KOH + H_2O$$

Submitted by H. T. Clarke and E. R. Taylor.
Checked by Henry Gilman and J. H. McGlumphy.

### 1. Procedure

In a 12-l. flask fitted with stirrer and reflux condenser are placed 600 g. (3.8 moles) of potassium permanganate, 7 l. of water and 200 g. (1.6 moles) of *o*-chlorotoluene (Org. Syn. 3, 33). The mixture is slowly heated to boiling (Note 1) with continual stirring, until the permanganate color has disappeared. This requires three to four hours. The condenser is now set downward for distillation and the mixture is distilled, with constant stirring, until no more oil passes over with the water. The unattacked *o*-chlorotoluene thus obtained amounts to 25–30 g. The hot mixture is filtered with suction and the cake of hydrated manganese dioxide washed with two 500-cc. portions of hot water. The combined filtrate is concentrated (Note 2) to about 3.5 l.; if it is not entirely clear it may be clarified by the use of 1–2 g. of decolorizing carbon. It is now, while still hot, acidified by cautiously adding 250 cc. of concentrated hydrochloric acid (sp. gr. 1.19) with continual agitation. When the mixture is cool the white precipitate of *o*-chlorobenzoic acid is filtered off and washed with cold water. The dry weight is 163–167 g. (74–78 per cent of the theoretical amount, based on the amount of *o*-chlorotoluene actually oxidized) of a very nearly pure (Note 3) product melting at 137–138°. For purification this may be recrystallized from 600 cc. of toluene, when 135–140 g. of a product melting at 139–140° is obtained. Further crops can be obtained by concentrating the mother liquor.

## 2. Notes

1. If the mixture is heated too rapidly the reaction may be violent at the outset. In such a case it can be controlled by laying wet towels upon the upper part of the flask.

2. This concentration is satisfactorily carried out on the steam bath under reduced pressure (Org. Syn. 4, 54).

3. Care must be taken to use pure *o*-chlorotoluene in this preparation; otherwise the *o*-chlorobenzoic acid may be contaminated with isomeric acids which are very difficult to remove. The *o*-chlorotoluene therefore should be prepared from pure *o*-toluidine or *o*-chlorotoluenesulfonic acid.

## 3. Methods of Preparation

The only practical methods of preparing *o*-chlorobenzoic acid consist in the oxidation of *o*-chlorotoluene and the replacement of the amino group in anthranilic acid by a chlorine atom. Both of these methods have been fully discussed by Graebe,[1] who recommends the former for the preparation of relatively large quantities. The oxidation of *o*-chlorotoluene by permanganate was originally described by Emmerling.[2]

[1] Graebe, Ann. **276**, 54 (1893).
[2] Emmerling, Ber. 8, 880 (1875).

## IX

# DIMETHYLGLYOXIME

$$C_2H_5OH + HNO_2(NaNO_2 + H_2SO_4) \rightarrow C_2H_5ONO + H_2O$$

$$C_2H_5ONO + CH_3COCH_2CH_3 \rightarrow CH_3COC{=}(NOH)CH_3 + C_2H_5OH$$

$$\begin{array}{l} CH_3C{=}O \\ \quad | \\ CH_3C{=}NOH \end{array} + NaO_3SNHOH \rightarrow \begin{array}{l} CH_3C{=}NOH \\ \quad | \\ CH_3C{=}NOH \end{array} + NaHSO_4$$

Submitted by W. L. Semon and V. R. Damerell.
Checked by Henry Gilman and R. E. Fothergill.

## 1. Procedure

*A. Ethyl Nitrite.*—Two solutions are prepared. Solution I contains 620 g. (9 moles) of sodium nitrite (650 g. of technical 95 per cent), 210 g. (4.57 moles) of alcohol (285 cc. of 90 per cent denatured, or its equivalent) and water to make a total volume of 2500 cc. Solution II contains 440 g. of sulfuric acid (255 cc. of sp. gr. 1.84) and 210 g. of alcohol, diluted with water to 2500 cc. Ethyl nitrite may be generated continuously in gaseous form by allowing solution II to flow into solution I.

The gas can be conveniently made by putting solution II in a 2.5-l. bottle fitted with a two-hole rubber stopper (Fig. 1) and provided with glass tubing as indicated in the diagram. The rate of flow of solution II into a 6-l. bottle containing solution I is regulated by a screw clamp. The ethyl nitrite generated flows out of the second opening in the stopper of the lower bottle. The stoppers to both bottles should be wired on. A mechanical stirrer in the lower bottle is helpful in securing a steady evolution of the gas (Note 1).

*B. Biacetyl Monoxime.*—In a 2-l. three-neck flask provided with a condenser, a thermometer and an inlet tube for ethyl

nitrite, and arranged for external cooling, is placed 620 g. (775 cc.) of commercial methyl ethyl ketone which has been dried with, and filtered from, 75 g. of anhydrous copper sulfate. Forty cc. of hydrochloric acid (sp. gr. 1.19) is added (Note 2) and the temperature raised to 40°. The ethyl nitrite from the preceding preparation is now bubbled in, the temperature being maintained between 40 and 55°. After all of the ethyl nitrite has been passed in (Note 3) the crude product may be used in the preparation of dimethylglyoxime by distilling off the alcohol formed in the reaction until the temperature of the liquid reaches 90° (Note 4).

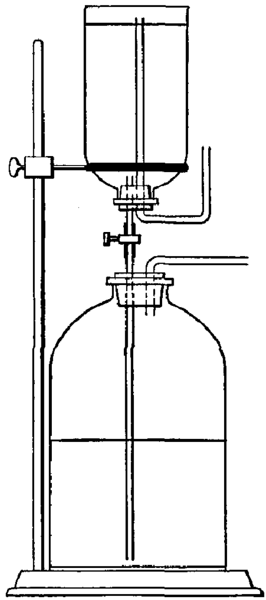


FIG. 1.

If pure biacetyl monoxime is desired, the crude product is neutralized with about 35 cc. of concentrated aqueous ammonia and diluted with half its volume of water. It is then distilled to remove alcohol, etc., until the distillate is no longer inflammable. The receiver is changed and the contents are now rapidly distilled, using superheated steam. Almost all of the biacetyl monoxime comes over in the first 5 l. of distillate. One to 1.5 kg. of salt is dissolved in the distillate, which is then cooled to 0°. The solid biacetyl monoxime crystallizes out and may be filtered off. The yield is 480–520 g. The product can be further purified, if desired, by recrystallizing from water (Note 5).

*C. Sodium Hydroxylamine Monosulfonate.*—In a 12-l. crock are mixed 5 kg. of shaved ice (Note 6) and 569 g. of sodium nitrite (594 g. of the technical 95 per cent quality). Into this is stirred a suspension of sodium bisulfite containing 1100 g. of available sulfur dioxide (about 1775 g. of technical bisulfite) in 750 cc. of water. Then, beneath the surface of the solution is added, with constant stirring, 150 cc. of glacial acetic acid

(Note 7) followed by a mixture of 550 cc. of concentrated hydrochloric acid (sp. gr. 1.19) with 400 g. of shaved ice (Note 8). The entire solution should always remain below 0°, further ice being added if there is a tendency for the temperature to rise. The solution should now become acid to Congo Red paper and contain 6 or more moles of the sodium hydroxylamine disulfonate, which rapidly hydrolyzes to an acid solution of the monosulfonate.

*D. Dimethylglyoxime.*—The crude biacetyl monoxime, remaining after distilling to 90° and containing about 5 moles of biacetyl monoxime, is added to the sodium hydroxylamine monosulfonate solution (which has been filtered to remove any sediment) and which is contained in a 15-l. flask. It is heated to 70° and allowed to remain warm (with occasional stirring) for several hours (Note 9). The dimethylglyoxime separates in crystals which can be filtered from the solution as soon as it has become cold (Note 10). The crystals are washed with cold water until free of sulfate. The yield of compound melting at 238–240° is 540–575 g.

Recrystallization is unnecessary since the product is pure white and free from tarry material (Note 5).

*E. Sodium Dimethylglyoximate.*—To a solution of 75 g. of sodium hydroxide in 300 cc. of water is added, with stirring, 100 g. of dimethylglyoxime (Note 11). Heat is applied to effect solution (Note 12), and the mixture is filtered from any slight residue. The solution is poured while hot into 500 cc. of 95 per cent alcohol. After cooling to 5°, with stirring, the crystals which form are filtered, then suspended in 150 cc. of alcohol and again filtered, and finally dried at 25° until the solid has no odor of alcohol (Note 13). The yield is 213–230 g. (81–88 per cent of the theoretical amount) of the octahydrate.

## 2. Notes

1. If a mechanical stirrer is not used care should be exercised to prevent a layer of solution II from collecting at the bottom of solution I, since under these conditions a little shaking produces too violent an evolution of gas.

Because ethyl nitrite is harmful if inhaled continuously, the reaction should be carried out in a hood or out of doors.

2. The methyl ethyl ketone should not be allowed to stand any length of time between the addition of the hydrochloric acid and the treatment with ethyl nitrite, inasmuch as the acid causes a condensation of the ketone with itself, thereby lowering the yield of biacetyl monoxime.

3. The ethyl nitrite may be passed into the solution as rapidly as possible, providing the temperature does not exceed 55°. Very complete absorption takes place, and the time of addition is about one and one-half hours.

4. Care should be taken that the distillation for the removal of alcohol and excess methyl ethyl ketone does not stop under 90° or go beyond this temperature. If stopped too soon, the alcohol that is not boiled off later increases the solubility of the dimethylglyoxime; and too high a temperature causes the formation of tarry products. Both of these factors reduce the yield.

5. About 70–80 per cent of the biacetyl monoxime is recovered on crystallization. Practically all of the monoxime left in the mother liquor can be recovered by steam distillation. The recrystallized and dried compound melts at 76.5°. Purification by distillation is not recommended.

The biacetyl monoxime turns brown rapidly after preparation and it must not be allowed to stand before adding it to the hydroxylamine monosulfonate in the preparation of dimethylglyoxime if this final product is to be obtained in a colorless condition.

6. Shaved ice is used in place of crushed ice because of more efficient cooling. The use of snow is advised, if it is available.

7. The acetic acid helps to buffer the solution and maintain a low hydrogen-ion concentration, which is favorable for a good yield.

8. The acid may be added as rapidly as desired so long as the temperature remains below 0° and no evolution of gas takes place. The entire addition should require not more than fifteen minutes.

9. The mixture is warmed to hasten the hydrolysis of disulfonate to monosulfonate, and also to increase the solubility of the biacetyl monoxime in the monosulfonate solution.

10. The dimethylglyoxime should not be filtered off until the mixture has become perfectly cool, because dimethylglyoxime is slightly soluble in a warm acid solution.

11. Crude or discolored dimethylglyoxime may be used since the impurities remain in solution in the aqueous alcohol.

12. The solution of dimethylglyoxime in sodium hydroxide should not be boiled, since prolonged heating causes decomposition.

13. The sodium salt may be further purified if desired by dissolving in water and reprecipitating with alcohol. Large crystals may be secured by crystallizing slowly from water.

Too long drying, or drying at too high a temperature, partially dehydrates the salt, with the result that it dissolves much more slowly in water and is therefore less desirable for making solutions for use in qualitative or quantitative analysis. Sodium dimethylglyoximate is extremely soluble in water. A 3 per cent (0.1 M) aqueous solution is suggested to replace the 1 per cent alcoholic solution now used in analytical work.

## 3. Methods of Preparation

Biacetyl monoxime has been prepared by the action of amyl nitrite on methyl ethyl ketone using sodium hydroxide[1] or hydrochloric acid[2] as a condensing agent, and by melting nitrosolevulinic acid.[3]

Dimethylglyoxime has been prepared by the action of hydrochloric acid upon biacetyl monoxime;[4] by the action of hydroxylamine on biacetyl;[5] by the action of hydroxylamine on biacetyl

[1] Claisen, Ber. **38**, 696 (1905).

[2] Diels and Farkas, Ber. **43**, 1957 (1910); Biltz, Z. anal. Chem. **48**, 164 (1909); Semon and Damerell, J. Am. Chem. Soc. **47**, 2038 (1925).

[3] Thal, Ber. **25**, 1720 (1892).

[4] Schramm, Ber. **16**, 180 (1883); Johlin, J. Am. Chem. Soc. **36**, 1218 (1914).

[5] Fittig, Daimler, and Keller, Ann. **249**, 182 (1888); Wolff, Ann. **288**, 1 (1895).

monoxime;[6] and by the action of sodium hydroxylamine monosulfonate on biacctyl monoximc.[7] It is formed in small amounts, together with ethylnitrolic acid, by the action of oxides of nitrogen upon methyl ethyl ketone.[8]

[6] Tschugaeff, Ber. **38**, 2520 (1905); Gandarin, J. prakt. Chem. (2) **77**, 414 (1908); Biltz, Z. anal. Chem. **48**, 164 (1909); Adams and Kamm, J. Am. Chem. Soc. **40**, 1281 (1918).

[7] Semon and Damerell, J. Am. Chem. Soc. **46**, 1290 (1924); **47**, 2033 (1925).

[8] Behrend and Tryller, Ann. **283**, 244 (1894).

# X

## DIPHENYLMETHANE IMINE HYDROCHLORIDE

$$8(C_6H_5)_2C{=}NOH \rightarrow$$
$$4(C_6H_5)_2CO + 4(C_6H_5)_2C{=}NH + N_2 + 2H_2O + 2NO$$
$$(C_6H_5)_2C{=}NH + HCl \rightarrow (C_6H_5)_2C{=}NH \cdot HCl$$

Submitted by ARTHUR LACHMAN.
Checked by C. R. NOLLER.

### 1. Procedure

A PIECE of glass tubing 80 cm. long and 2 cm. in internal diameter is sealed at one end and loosely packed with 49 g. (0.25 mole) of benzophenoneoxime (p. 10). The tube is supported in a nearly horizontal position, dipping slightly toward the closed end, and connected to a small filter flask by means of rubber stoppers and a piece of glass tubing bent at a right angle. The system is evacuated by means of a water pump and dry carbon dioxide admitted, re-evacuated, and carbon dioxide admitted again. The oxime is then heated with a free flame beginning at the upper end and heating at one spot until decomposition takes place before heating a further portion (Note 1). When all of the oxime has been decomposed, the mixture which has collected at the closed end of the tube (Note 2) is heated strongly for a short time to complete the decomposition, and allowed to cool. Suction is again applied to the tube and the condensed water is driven out by gently warming the tube. The liquid is then transferred to a small distilling flask and distilled at a pressure of about 20 mm. The distillate, consisting of a mixture of benzophenone and diphenylmethane imine, is dissolved in 400 cc. of ligroin (60–90°) and the imine hydrochloride is precipitated by bubbling in dry hydrogen chloride. The salt is filtered with suction (Note 3), washed with a little ligroin, dried, and pre-

served in a dry atmosphere (Note 4). It sublimes without decomposition at 230–250° (Note 5). The yield is 16–18 g. (59–66 per cent of the theoretical amount) (Note 6).

## 2. Notes

1. When the heating is carefully done, no material is carried out of the tube with the gases.

2. Care should be taken to prevent any drops of water that have condensed in the cool portion of the tube from running back and mixing with the liquid that is being heated.

3. Benzophenone may be recovered from the filtrate.

4. In moist air the hydrochloride is changed to a mixture of benzophenone and ammonium chloride. The free base on standing in air gives off ammonia and gradually deposits crystals of benzophenone.

5. The imine salt can be converted into the free base by the method of Hantzsch and Kraft, which involves treating a solution of the salt in chloroform with dry ammonia.

6. The yield depends greatly on the quality of the benzophenoneoxime. If this contains moisture or has been exposed to moist air, especially in a closed space, for any length of time, the yield is markedly decreased.

## 3. Methods of Preparation

Diphenylmethane imine (or its hydrochloride) has been obtained by heating diphenyldichloromethane with urethane at 130°;[1] by the action of ammonia on diphenyldibromomethane;[2] by treating benzophenonechloroimide with phosphorus pentachloride in ether solution,[3] or dry hydrogen chloride in ligroin solution;[4] by the action of phenylmagnesium bromide on *N*-bromobenzamide,[2] benzonitrile,[5] cyanogen bromide,[6] cyano-

[1] Hantzsch and Kraft, Ber. **24**, 3516 (1891).

[2] Moore, Ber. **43**, 564 (1910).

[3] Vosburgh, J. Am. Chem. Soc. **38**, 2095 (1916).

[4] Peterson, Am. Chem. J. **46**, 331 (1911).

[5] Moureu and Mignonac, Compt. rend. **156**, 1806 (1913); Ann. Chim. (9) **14**, 336 (1920).

[6] Grignard, Bellet and Courtot, Ann. chim. (9) **4**, 34 (1915).

gen chloride,[7] and alkyl thiocyanates.[8] It has also been obtained by passing a mixture of ammonia and benzophenone vapor over thorium oxide at 380–390°;[9] by the catalytic reduction of benzophenoneoxime using hydrogen and a nickel catalyst in absolute alcohol solution at ordinary temperature and pressure;[10] by passing a mixture of hydrogen and benzophenoneoxime vapor over reduced copper at 200°;[11] and by the action of sodium ethylate on *N*-monochlorodiphenylmethylamine in alcoholic solution.[12] The method described here has been previously published by Lachman.[13]

[7] Grignard, Bellet and Courtot, Ann. chim. (9) **12**, 379 (1919).

[8] Adams, Bramlet and Tendick, J. Am. Chem. Soc. **42**, 2372 (1920).

[9] Mignonac, Compt. rend. **169**, 239 (1919).

[10] Mignonac, Compt. rend. **170**, 938 (1920).

[11] Yamaguchi, Bull. Chem. Soc. Japan **1**, 35 (1926) [C. A. **21**, 75 (1926)].

[12] Hellerman and Sanders, J. Am. Chem. Soc. **49**, 1742 (1927).

[13] Lachman, J. Am. Chem. Soc. **46**, 1477 (1924).

# XI

## DURENE

(1,2,4,5-*Tetramethyl benzene*)

(By-products, Penta- and Hexa-methyl benzenes)

$$C_6H_4(CH_3)_2 + 2CH_3Cl \xrightarrow{AlCl_3} C_6H_2(CH_3)_4(1,2,4,5) + 2HCl$$

Submitted by LEE IRVIN SMITH.
Checked by F. C. WHITMORE and THOS. E. HOLLINGSHEAD.

### 1. Procedure

A 5-l. flask, mounted on a steam bath, is fitted with a wide (Note 1) inlet tube reaching to the bottom of the flask, a reflux condenser, and a delivery tube running from the top of the reflux condenser and reaching to the bottom of a heavy glass cylinder containing a column of mercury about 10 cm. high. All stoppers and joints of the apparatus must fit tightly and be wired, as the reaction is carried out under a slight pressure. In the flask are placed 3180 g. (3700 cc., 30 moles) of xylene (Note 2) and 1000 g. of anhydrous aluminium chloride (Note 2). The inlet tube of the flask is then connected to a tank of methyl chloride or to a methyl chloride generator (Note 3), the steam is turned on in the bath, and a fairly rapid stream of methyl chloride is passed into the mixture (Note 4). At first there will be a rapid absorption, and the stream of gas must be regulated so that the mercury in the pressure tube does not tend to suck back. The hydrogen chloride formed may be conveniently disposed of by a trap devised by Johnson (Org. Syn. **8**, 27, Note 2). As the reaction slows down, the pressure increases until both hydrogen chloride and methyl chloride begin to escape through the mer-

cury. At this point the current of incoming gas should be cut down so that undue loss of methyl chloride is avoided. About one hundred hours are required for the completion of the reaction (Note 5).

When the reaction is completed, the steam is turned off and the flask is disconnected and loosely stoppered. After standing over night the reaction mixture is decomposed by pouring it slowly into 5 kg. of chopped ice. The greenish oil which separates from the aqueous layer is removed, dried over calcium chloride, filtered and fractionated twice, using a round-bottom flask fitted with an efficient column and an air condenser (Note 6).

The fractions are cut as follows:

| Fraction | Temp. Range | Distillate | Yield, g. |
|---|---|---|---|
| I and II | Up to 150° | Benzene, xylene | little |
| III | 150 to 180 | Trimethyl benzenes | 570 |
| IV | 180 to 205 | Tetramethyl benzenes | 2075 |
| V | Above 205 | Mostly pentamethyl benzene | 815 |

Typical yields of the various fractions are given in the table; they may vary 10 to 20 per cent from these figures, owing to slight differences in procedure and materials, and especially to differences in the quality of the aluminium chloride employed. The more efficient this material is, the greater the percentage of the higher boiling fractions.

The tetramethyl benzene fraction (IV) is rich in durene, which may be frozen out and filtered off because of its relatively high melting point (80°). To isolate the durene, fraction IV is thoroughly chilled in an ice-calcium chloride pack, and filtered off through a cold filter (Note 7) using good suction, and pressing down the solid compactly. When no more liquid drips through the cold filter, the filtration apparatus is allowed to come gradually to room temperature (Note 7) and the suction is continued as long as any liquid drips through, after which the solid is removed and bottled. The yield is 540 to 610 g.

Fraction III may be methylated to the tetramethyl benzene stage by heating on the steam bath with 100 g. of anhydrous aluminium chloride and passing in 225 g. of methyl chloride. The filtrates from the durene likewise yield more durene when heated

on the steam bath with 50 g. of aluminium chloride. The products are worked up in the usual way, that is, they are decomposed by pouring into twice their weight of chopped ice, separated from the aqueous layer, fractionated twice, and the durene frozen out as before. By conducting one methylation of the trimethyl benzene fraction, and one treatment of the durene filtrates, the combined yield of crude durene will average 1000 to 1400 g. (25–35 per cent of the theoretical amount based on the original 30 moles of xylene).

To purify the durene, 200 g. of the crude product is placed in a 1-l. round-bottom flask fitted with a reflux condenser, and melted in a water bath at 95°; 200 cc. of warm (50°) 95 per cent ethyl alcohol is then added through the top of the condenser, and the mixture is carefully heated until homogeneous. The solution is filtered on a hot-water funnel, allowed to stand tightly covered (Note 8) in a fairly warm place (35°) over night, cooled to about 0°, and filtered on a suction filter. The product (about 169 g.) melts at 74–78°. A second recrystallization yields 149 g. melting at 77–79°. A third recrystallization yields 140 g., having a melting point of 79–80°. The alcoholic filtrates are fractionated and the crude durene obtained is worked over with the isomers of durene.

*Pentamethyl benzene.*—Fraction V, and xylene which is methylated beyond the tetramethyl benzene stage, may be worked up for pentamethyl benzene. If xylene is to be methylated to obtain pentamethyl benzene, one more mole of methyl chloride should be used, and the mixture of xylene and anhydrous aluminium chloride methylated for one hundred and ten hours instead of the one hundred used for durene. Otherwise the procedure is exactly the same as for durene. The reaction mixture is decomposed and fractionated in the usual way, and the material boiling above 205° (fraction V) is separated into three fractions:

| Fraction | Temperature Range | |
|---|---|---|
| VI | 205–215° | Tetra- and pentamethyl benzene |
| VII | 215–235 | Mostly pentamethyl benzene |
| VIII | Residue above 235 | Hexamethyl benzene and tars |

The pentamethyl benzene obtained in this way is nearly pure, and one recrystallization from 95 per cent alcohol or from a mixture of equal volumes of alcohol and benzene gives a snow-white product, but the product generally melts over too wide a range for practical purposes. However, if fraction VII is refractionated under diminished pressure and the fraction boiling at 123–133°/22 mm. (practically all at 127–129°) is collected and recrystallized as in the following paragraph, a product melting quite sharply at 52° (true m.p. 53°) is obtained.

Six hundred grams of crude pentamethyl benzene is heated to 100° and poured slowly with stirring into 1000 cc. of 95 per cent ethyl alcohol heated to 70° in a 2-l. beaker, and allowed to stand over night at a temperature of approximately 30°. The crystals formed are collected on a suction filter and dried at room temperature over night on a porous plate. The yield is about 250 g. (Note 9).

*Hexamethyl benzene.*—Fraction VIII is fractionated in 250-cc. batches in a Claisen flask at 20 mm. pressure, the following fractions being collected:

| Fraction | Temperature Range | |
|---|---|---|
| IX | 80–110° | Mostly tetra- and pentamethyl benzenes |
| X | 110–135 | Mostly pentamethyl benzene |
| XI | 135–170 | Hexamethyl benzene |
| XII | Residue above 170 | Hexamethyl benzene and tars |

This fractionation may be carried out in an ordinary Claisen flask, but there is some difficulty in maintaining the desired pressure due to the solvent action of the hydrocarbons on the rubber stopper. This difficulty may be avoided by the use of a Claisen flask with very long necks and a wide side-tube. The material should be distilled fast enough to prevent it from solidifying in the column and side tube. Prolonged heating of hexamethyl benzene also causes a considerable amount of decomposition to tars.

The method for the production of large amounts of hexamethyl benzene is the rapid methylation of pentamethyl benzene or the durene filtrates. A mixture of 378 g. of pentamethyl benzene and 200 g. of anhydrous aluminium chloride is heated

on an oil bath at 190–200° and a rapid stream of dry methyl chloride is bubbled through for three to four hours, using the same apparatus as was used for the preparation of durene. The mixture is allowed to stand over night at room temperature. One liter of hot xylene is added to dissolve the solidified material, and the reaction mixture is decomposed by pouring it onto 3 kg. of chopped ice. The resulting oil is separated and the xylene and other low boiling material is removed by distillation under reduced pressure (Note 10). The fractions are divided as above. Two refractionations and two recrystallizations (Note 11) give 98–121 g. of white crystals, melting at 157–161° (Note 12).

## 2. Notes

1. The inner tube of a condenser makes a good inlet tube. It should be placed so that the wide end is inside the large flask.

2. The xylene should be a good, colorless laboratory grade, b.p. 135–140°. Any moisture present may be removed by distilling and discarding the first 10 per cent of the distillate. The best aluminium chloride available should be used, for the methylation is very unsatisfactory if the catalyst is of an inferior grade. It should be in small pieces, but need not be powdered.

3. The methyl chloride generator consists of a 5-l. flask resting on a sand bath and fitted with a reflux condenser, with a delivery tube running from the top of the condenser to a train of wash bottles, two containing water and two containing concentrated sulfuric acid, with three safety bottles, one at each end of the train, and one between the water and sulfuric acid bottles. To charge for about 45 moles (theoretical) of methyl chloride: 200 g. of water and 2200 g. (1200 cc.) of concentrated sulfuric acid are placed in the flask, and 1400 g. (1760 cc.) of methyl alcohol is added, with cooling, at such a rate that the temperature does not rise above 70°. Then 2400 g. of sodium chloride is added, the apparatus is tightly connected, and the flask heated on the sand bath so that the gas is evolved at a fairly rapid rate. It has been found in practice that, using materials of the commercial grade, the yield of methyl chloride is about 55 to 65 per

cent of the theoretical amount, so that about double the calculated quantities must be used. This means that the generator has to be charged three times in order to convert 30 moles of xylene to tetramethyl benzene. If a tank of methyl chloride is available, 65–70 moles of methyl chloride should be used for this same amount of xylene. The tank should be weighed before starting and the reaction stopped when the tank has lost the proper amount in weight.

4. Experiments have shown that the rapid current of methyl chloride furnishes sufficient stirring.

5. The normal time of one hundred hours can be shortened by increasing the amount of aluminium chloride. The product in this case, however, is very viscous and rather difficult to handle in large amounts.

6. Two systematic fractionations (not redistillations) with a good column are absolutely necessary in order to obtain good separations. The more efficient the column the better.

7. The material should be filtered through a large Büchner funnel, which is immersed in a freezing mixture as long as any liquid drips through. It is stated in the literature that the first filtrate obtained in this way is mostly isodurene (1,2,3,5–), whereas the second filtrate, obtained as the material warms slowly to room temperature, is pseudodurene or prehnitene (1,2,3,4–), m.p. $-4°$.

8. Durene is quite volatile, and should not be allowed to remain exposed to the air any longer than necessary. It is also quite volatile with alcohol, and the mother liquors resulting from the recrystallizations should be distilled: the alcoholic distillate is used for further recrystallizations, and the residues may be worked up for durene by heating with aluminium chloride.

9. The melting point of pentamethyl benzene is only slightly affected by recrystallization, because most of the impurity is hexamethyl benzene, which can be removed only by fractionation.

10. Hexamethyl benzene decomposes when heated very strongly for any length of time. Better results are therefore obtained if the distillations are carried out under reduced pressure.

11. Small amounts of impurities greatly influence the melting point of hexamethyl benzene, and several recrystallizations of a fraction of close boiling range are necessary in order to prepare a sharply melting product.

12. Small amounts (25 g. or less) of hexamethyl benzene which is nearly pure, are best recrystallized from ethyl alcohol. It requires about 600 cc. of boiling alcohol to dissolve 25 g., but on cooling 20 g. of pure product will result. Ether and benzene dissolve the substance much more readily, and larger amounts of materials are best recrystallized from either of these solvents, or from a mixture of one of them with alcohol. 125 g. of the hexamethyl benzene distillate which has been refractionated is melted and poured slowly with stirring into 1500 cc. of 95 per cent alcohol. A small amount remains undissolved and may be brought into solution by adding about 300 cc. of hot benzene, the beaker being heated on a steam bath and the mixture stirred constantly until all is dissolved. The solution is allowed to stand over night at approximately 25°. The crystals are filtered off by suction and washed with enough 95 per cent alcohol to moisten thoroughly (about 25 cc.). After drying, the crystals weigh approximately 112 g. and melt at 155–159°.

## 3. Methods of Preparation

Durene, pentamethyl benzene and hexamethyl benzene have usually been prepared from benzene or one of its methylated derivatives by the Friedel-Crafts synthesis.[1] Durene has been made from bromine derivatives of methylated benzenes by the Fittig reaction.[2] It has also been obtained in 20 per cent yield by passing methyl alcohol and acetone vapors over heated alu-

[1] Ador and Rilliet, Ber. **12**, 331 (1879); Friedel and Crafts, Compt. rend. **91**, 257 (1880); Ann. chim. phys. (6) **1**, 449 (1884); Jacobsen, Ber. **14**, 2629 (1881); **18**, 338 (1885); **20**, 896 (1887); Anschütz, Ann. **235**, 185 (1886); Claus and Foecking, Ber. **20**, 3097 (1887); Beaurepaire, Bull. soc. chim. **50**, 676 (1888).

[2] Jannasch and Fittig, Z. Chem. **13**, 161 (1870); Jannasch, Ber. **7**, 692 (1874); **10**, 1354 (1877).

minium oxide.[3] Hexamethyl benzene has been obtained by the action of zinc chloride on methyl alcohol [4] or on acetone.[5] The method given in the procedure has recently been described in the literature.[6]

[3] Reckleben and Scheiber, Ber. **46**, 2363 (1913).

[4] LeBel and Greene, Compt. rend. **87**, 260 (1878).

[5] Greene, Compt. rend. **87**, 931 (1878).

[6] Smith and Dobrovolny, J. Am. Chem. Soc. **48**, 1413 (1926).

# XII

## DUROQUINONE

$$C_6H_2(CH_3)_4(1,2,4,5) \rightarrow C_6(CH_3)_4(NO_2)_2$$

$$2C_6(CH_3)_4(NO_2)_2 \xrightarrow{SnCl_2+HCl} [C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4$$

$$[C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4 \xrightarrow{FeCl_3} 2C_6(CH_3)_4O_2$$

Submitted by LEE IRVIN SMITH.
Checked by F. C. WHITMORE and THOS. E. HOLLINGSHEAD.

### 1. Procedure

*A. Dinitrodurene.*—A solution of 13.4 g. (0.1 mole) (Notes 1,2) of durene (p. 32) in 100 cc. of chloroform is added to 75 cc. of concentrated sulfuric acid in an 800-cc. beaker provided with a thermometer and an efficient mechanical stirrer. The mixture is cooled to 10°, and 16 g. (10.7 cc.) of fuming nitric acid (sp. gr. 1.5) (Note 3) is added drop by drop, with stirring, from a 125-cc. separatory funnel, the mixture being cooled in an ice-salt bath and the nitric acid added at such a rate that the temperature does not rise above 50° (about fifteen minutes is required for the addition). As soon as all the acid has been added the mixture is poured into a separatory funnel, the sulfuric acid layer is removed and the upper chloroform layer is immediately (Note 4) run into 500 cc. of 10 per cent sodium carbonate solution. The sulfuric acid layer is discarded because it contains very little dinitrodurene. Four portions are nitrated and the combined chloroform solutions are washed twice with 2.5 per cent sodium carbonate solution, dried over night with 30 g. of anhydrous calcium chloride, filtered, and the chloroform distilled off until crystals of dinitrodurene begin to appear. At this point four times the volume of hot 95 per cent ethyl alcohol is added (about

500 cc.), and the resulting mixture is cooled to 10°. The solid is filtered and washed twice with 50 cc. of cold (10°) 95 per cent ethyl alcohol. The yield from four nitrations is 82.5–84 g. (92–94 per cent of the theoretical amount) of a product melting at 207–208°.

*B. Reduction of Dinitrodurene.*—A solution of 90 g. of dinitrodurene in 1 l. of glacial acetic acid is boiled in a 12-l. flask (Note 6); 700 g. of stannous chloride is dissolved in 800 cc. of concentrated hydrochloric acid and heated to boiling. The heat is removed from the acetic acid solution of the nitro compound, and the stannous chloride solution is poured very carefully (during about ten minutes) into the dinitrodurene solution. The reaction is complete in fifteen minutes, and as the solution cools the stannic chloride compound of the diamine begins to crystallize. The reaction mixture is cooled to 10° in an ice-water bath, and the solid is filtered off by suction, washed twice with 50 cc. of 95 per cent ethyl alcohol and twice with 50 cc. of ether, and dried. The filtrates from the tin compound contain very little of the reduction product and may be discarded. The composition of this compound is $[C_6(CH_3)_4(NH_2 \cdot HCl)_2]_2 \cdot SnCl_4$, and it crystallizes from the reaction mixture in fine, glistening plates which are almost colorless. The yield is 145 g. (97 per cent of the theoretical amount).

*C. Duroquinone.*—A suspension of 100 g. of the tin compound in a solution of 300 g. of ferric chloride crystals in a mixture of 150 cc. of water and 20 cc. of concentrated hydrochloric acid is allowed to stand over night at about 30°, and is then filtered. The product is dissolved in 150 cc. of hot 95 per cent ethyl alcohol. The solution is filtered and allowed to stand over night at 30°. The yield is 40 g. of duroquinone (90 per cent of the theoretical amount) melting at 109–110°.

## 2. Notes

1. It is better to nitrate the durene in small batches, for a high yield and pure product depend upon not allowing the reaction mixture to remain in contact with the nitric acid very long.

2. Pure durene is absolutely essential for good results. It should be recrystallized from methyl alcohol until the melting point is 79–80°.

3. A large excess of nitric acid is undesirable, since it lowers the yield. The concentration of the nitric acid is also of importance, and to obtain the best results, it should have a specific gravity of 1.5 or more.

4. It is important that the chloroform layer be run into the carbonate solution as quickly as possible, for continued standing while in contact with even small amounts of acid leads to the formation of considerable amounts of red, tarry material. This renders the subsequent purification of the nitro compound much more difficult.

5. No mononitrodurene is ever obtained in this process. Either the dinitro compound results, or else unchanged material and oxidation products.

6. A large flask is necessary because the reduction is vigorous and the reaction mixture will boil up and practically fill the flask of the size recommended.

### 3. Methods of Preparation

Duroquinone, tetramethyl-*p*-benzoquinone, has been prepared in three ways: by the condensation of 2, 3-diketopentane with itself in the presence of alkalies,[1] by the action of alkalies on 3,3-dichloropentanone-2,[2] by means of the series of reactions used in these directions,[3] which is due originally to Nef.[4] The method of nitration used in preparing dinitrodurene according to these directions is a modification of a method of nitration first used by Willstätter.[5]

[1] von Pechmann, Ber. **21**, 1420 (1888).
[2] Faworsky, J. prakt. Chem. (2) **51**, 538 (1895).
[3] Smith and Dobrovolny, J. Am. Chem. Soc. **48**, 1420 (1926).
[4] Nef, Ber. **18**, 2806 (1885); Ann. **237**, 5 (1887).
[5] Willstätter, Ber. **42**, 4151 (1909).

## XIII

## ERUCIC ACID

$$CH_3(CH_2)_7CH{=}CH(CH_2)_{11}CO_2H$$

(Hydrolysis of Rape Seed Oil)

Submitted by C. R. NOLLER and R. H. TALBOT.
Checked by H. T. CLARKE and E. R. TAYLOR.

### 1. Procedure

IN a 5-l. flask fitted with a reflux condenser are placed 2500 cc. of 95 per cent ethyl alcohol and 340 g. (4.5 moles) of commercial (73–75 per cent) potassium hydroxide. The mixture is gently shaken until the hydroxide is dissolved, 1330 g. (1500 cc., approximately 4 equivalents) of rape seed oil is added with shaking (Note 1) and the mixture is refluxed on a steam bath for twenty-five to thirty hours.

The hot mixture is poured, with stirring, into 15 l. of warm water (50–60°), and is followed by 700 cc. (8.2 moles) of concentrated (36 per cent) hydrochloric acid (Note 2). After standing until the layers are distinct (ten to fifteen minutes), the lower layer is siphoned off as completely as possible and the oil is washed with two 1-l. portions of warm water.

The oil thus obtained, which should amount to 1460–1600 cc., is dissolved in three times its volume of 95 per cent ethyl alcohol and the mixture cooled to −10 to 0°, when the erucic acid crystallizes (Note 3). After six to eight hours at this temperature, the crude erucic acid is collected on a basket centrifuge (Note 4). The mother liquor, on chilling, yields a second crop of erucic acid. The combined product (800–1100 g.) melts either partially or wholly at room temperature, owing to the presence of oleic acid. It is dissolved in an equal volume of alcohol,

chilled for six hours at 0°, and centrifuged as before, when it is obtained in well-defined crystalline form. The second crop of this recrystallization resembles that of the first crystallization and must again be recrystallized. The product is finally recrystallized once again from an equal volume of 95 per cent alcohol. The recrystallized acid contains alcohol, which is removed by heating to constant weight on the steam bath under diminished pressure. The yield (Note 5) of acid obtained is 260–360 g.; it melts at 31–32° (Note 6).

## 2. Notes

1. If the solution is mixed in this manner, the rape seed oil emulsifies on being poured into the alkali and refluxing begins more smoothly.

2. If the acid is added before the water, esterification occurs to an appreciable extent, so that the yield may fall to less than 200 g.

3. The crystallization is best accomplished by cooling for several hours at 0°. Cooling in an ice-salt mixture is much quicker but the erucic acid so obtained contains more oleic acid.

4. The centrifuge affords an easy way of filtering the erucic acid, since, if the acid is not quickly separated from the mother liquor, it melts and makes separation impossible. If a centrifuge is not available, the acid must be filtered at 0°, which is inconvenient except during cold weather.

5. The mother liquors from the recrystallizations may be combined, evaporated, and distilled under reduced pressure, taking two equal fractions. The lower (b.p. 200–220°/5 mm.) consists mainly of oleic acid; the higher (b.p. 220–230°/5 mm.) is solid at 20° and yields a further quantity of erucic acid on recrystallization.

6. The acid obtained contains a small percentage of arachidic acid and other higher saturated fatty acids, and has an iodine number of 66.9 (instead of about 75). If not entirely colorless, the product may be distilled under reduced pressure, when it boils at 241–243°/5 mm. or 252–254°/12 mm.; there is practically

no loss, only a minute amount of higher boiling material remaining in the flask.

### 3. Methods of Preparation

Erucic acid is a constituent of various natural oils but is most conveniently obtained from rape seed oil. The process described above is essentially that of Reimer and Will.[1] Methods have been developed for obtaining pure erucic acid free from saturated acids,[2] but these involve time-consuming procedures of fractional precipitation and crystallization, and necessarily give poor yields. The product obtained above is satisfactory for most purposes.

[1] Reimer and Will, Ber. **19**, 3320 (1886).

[2] Holde and Wilke, Z. angew. Chem. **35**, 105, 186, 289 (1922); Täufel and Bauschinger, *ibid.* **41**, 157 (1928).

XIX

## ETHYL FUMARATE

$$\begin{matrix} HCCO_2H \\ \| \\ HO_2CCH \end{matrix} + 2C_2H_5OH \rightarrow \begin{matrix} HCCO_2C_2H_5 \\ \| \\ C_2H_5O_2CCH \end{matrix} + 2H_2O$$

Submitted by B. B. Corson, Elizabeth Adams, and R. W. Scott.
Checked by Henry Gilman and J. B. Dickey.

### 1. Procedure

The apparatus is assembled as shown in Fig. 2. Alcohol vapor from vaporizer flask *E* is passed through the acid contained in esterification flask *J*. The ester which is formed remains in *J* whereas the excess alcohol and the water formed during esterification continuously distil through column *K* into condenser *L* (Note 1). Flask *E* is a 250-cc. Pyrex distilling flask equipped with an extra side-arm *D*. Alcohol is run from dropping funnel *F* into flask *E*, a sufficient head being maintained by the height of funnel *G*. Stopcock *G′* is kept open, the flow of alcohol being regulated by stopcock *F′*. Side-arm *H* may be wrapped with asbestos paper to lessen condensation.

Side-arm *D* connects with two mercury safety valves, *C* and *B*. Tube *C′* dips about 3 cm. under the surface of the mercury contained in test tube *C*. This valve guards against excess internal pressure sometimes caused by the plugging of delivery tube *I*. Loud bubbling in the mercury quickly results from any clogging (Note 2) in the apparatus. Glass tube *A* (preferably a large capillary) barely dips into the mercury which just seals the bend of U-tube *B*. This valve guards against any fall of pressure within the system (Note 3), which would result in the transfer of the contents of flask *J* into vaporizer *E*, were it not compensated by the inrush of air through *A*. Since there is some lag

in this pressure compensation, the alcohol vapor delivery tube *I* should be about 30 cm. long; it should reach to within 2 or 3 cm. of the bottom of flask *J* and should extend about 10 cm. above the stopper of the flask. The delivery end may be drawn out to a coarse capillary (Note 4).

Esterification flask *J* is a 1-l. Pyrex round-bottom flask fitted with a 3-hole rubber stopper, carrying thermometer *T*, delivery

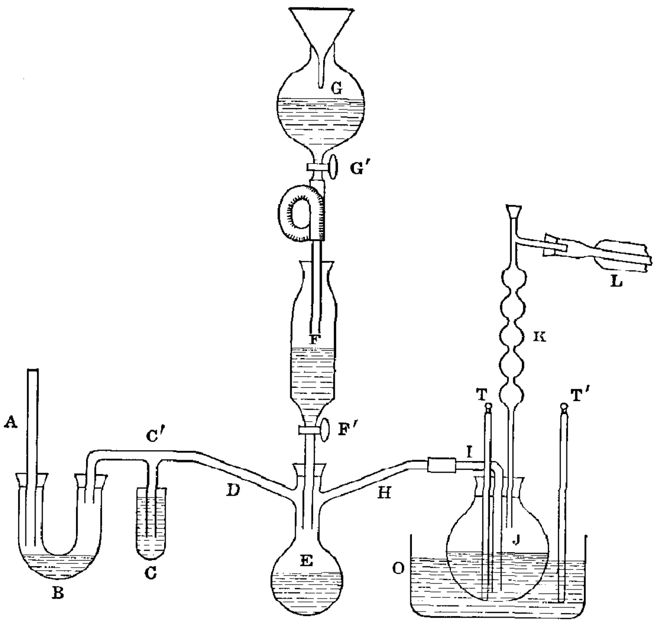



FIG. 2.

tube *I* and column *K*. Thermometer *T* should reach to within a few centimeters of the bottom of the flask, so as to register the temperature of the liquid esterification mixture. Flask *J* is immersed in and heated by the oil contained in deep dish *O*. Thermometer *T′* dips into the oil bath. Fractionating column *K* (Note 5) leads the vapor mixture of alcohol and water into condenser *L*.

Esterification flask *J* is charged with 348 g. (3 moles) of

fumaric acid and 350 cc. (Note 6) of 96 per cent ethyl alcohol containing 15 cc. of concentrated sulfuric acid. The oil bath is heated until the temperature of the reaction mixture in *J* is 110° (Note 7). During the preliminary heating about 200 cc. of alcohol distils from *J*. Then vaporizer *E* is heated over a gauze by a flame and the flow of 96 per cent (Note 8) alcohol (Note 9) from dropping funnel *F* is so regulated that the temperature of the esterification mixture in *J* remains between 115° and 120°, the temperature of the oil bath being maintained at about 150°. The reaction is stopped when 910 cc. of distillate has been collected; this requires about two hours.

The reaction mixture is then cooled to room temperature and neutralized with sodium carbonate solution (Note 10). The ester is separated and the aqueous layer shaken with benzene (Note 11); the liquids are combined, the benzene is distilled through a fractionating column (Note 12), and the ester from a side-arm flask at ordinary pressure, and the portion boiling at 213–215° is collected. The yield is 410 g. (80 per cent of the theoretical amount) (Note 13).

## 2. Notes

1. This preparation avoids the two disadvantages of the ordinary method of esterification by removing the water from the esterification mixture and by raising the reaction temperature.

2. If tube *I* clogs, the solid can often be blown out by temporarily raising test tube *C*, thereby increasing the pressure within the system.

3. Too rapid an addition of alcohol to *E* might cause a sudden fall of pressure.

4. The capillary tube *I* which delivers into flask *J* should be coarse, so as not to clog. With salicylic acid, which is especially prone to plug the delivery tube, the capillary end is omitted.

5. If a simple bent tube is used instead of a column, as much as 10 per cent of the ester may be carried over with the alcohol-water vapor.

6. The amount of alcohol to be added depends upon the

solubility of the acid in question. The esterification mixture when hot should be liquid enough to allow passage of the alcohol vapor. There should be no attempt to dissolve the acid completely. Complete solution occurs only after the esterification reaction has run for some time.

7. Should the acid tend to clog the delivery tube it is advisable to pass a slow stream of alcohol vapor through the esterification flask, in order to keep the tube open, even before the temperature of the esterification mixture has reached 110°.

8. If 99 per cent alcohol is used instead of 96 per cent, the yield of ethyl fumarate is 87 per cent of the theoretical instead of 80 per cent. When large quantities of ester are being prepared it is easy to use dry alcohol, since the alcohol-water distillate can be dehydrated over quicklime and used again. The wet alcohol is conveniently dehydrated by refluxing six hours over quicklime in a 12-l. flask and then distilling.

9. Methyl esters are easily prepared by substituting methyl for ethyl alcohol.

10. Sometimes a white solid precipitates when sodium carbonate solution is shaken with the esterification mixture. This solid usually dissolves if some water is added.

11. If the benzene solution of ester is to stand several hours before distillation it should be dried with a small amount of anhydrous sodium carbonate.

12. If the benzene is distilled from an ordinary distilling flask or through a simple bent tube some of the ester passes over with the benzene. The ester-benzene should be heated until the temperature at the top of the column is 110°.

13. This apparatus can be used in the preparation of various high boiling esters. Its development was assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

Following are the percentage yields obtained in the preparation of other esters; ethyl maleate, 73; ethyl salicylate, 70; ethyl oxalate, 80; ethyl benzoate, 92; methyl benzoate, 87. In the preparation of ethyl maleate troublesome emulsions were encountered in working up the product. Occasionally this hap-

pened with other esters. These emulsions can usually be broken by suction filtration. Salicylic acid esterifies more slowly than fumaric and requires a larger excess of alcohol.

### 3. Methods of Preparation

Various methods[1] of esterification, similar to the one described in the procedure, are to be found in the literature. In some methods[2] the process has been made continuous by passing the alcohol-water distillate through a dehydrator and then returning the vapor of the dried alcohol to the esterification mixture; in others,[3] a substance such as carbon tetrachloride, chloroform or benzene has been added, the water then being removed by means of a ternary mixture, for example, water-alcohol-benzene. When alcohol vapor is passed through the esterification mixture, as described above, the reaction temperature can be held as high as desired. The high temperature and the removal of water as fast as formed more than compensate for the absence of a large excess of alcohol.

Ethyl fumarate has been prepared from fumaric acid and ethyl alcohol, with or without sulfuric acid as catalyst,[4] from silver fumarate and ethyl iodide,[5] from silver maleate and ethyl iodide plus a trace of iodine,[6] from ethyl maleate by the action of iodine,[6] from ethyl maleate and phosphorus pentachloride,[7] and by passing hydrogen chloride into a boiling absolute alcohol solution of malic acid.[8]

[1] Lea, Am. J. Sci. (2) **39**, 210 (1865); Frankland and Duppa, Phil. Trans. Roy. Soc. London **156**, 310 (1866); Phelps and Hubbard, Am. J. Sci. (4) **23**, 368 (1907); Phelps and Phelps, Am. J. Sci. (4) **24**, 194 (1907); Kohler and Allen, Org. Syn. **3**, 54 (1923).

[2] Frankland and Aston, J. Chem. Soc. **79**, 517 (1901); Gibson, Proc. Roy. Soc. Edinburgh **28**, 703 (1908); Kenyon, Org. Syn. **5**, 59 (1925).

[3] Taylor, Proc. Roy. Soc. Edinburgh **25**, 831 (1905); Clarke and Davis, Org. Syn. **2**, 23 (1922); Wahl, Bull. soc. chim. (4) **37**, 715 (1925).

[4] Laubenheimer, Ann. **164**, 294 (1872); Purdie, J. Chem. Soc. **39**, 346 (1881); **47**, 856 (1885).

[5] Anschütz, Ber. **11**, 1645 (1878); **12**, 2282 (1879); Purdie, J. Chem. Soc. **39**, 346 (1881).

[6] Anschütz, Ber. **12**, 2282 (1879).

[7] Henry, Ann. **156**, 177 (1870).

[8] Laubenheimer, Ann. **164**, 295 (1872).

## ETHYL OXOMALONATE *

$$CH_2(CO_2C_2H_5)_2+2N_2O_3 \rightarrow CO(CO_2C_2H_5)_2+4NO+H_2O$$

Submitted by B. B. Corson and R. K. Hazen.
Checked by F. C. Whitmore and F. L. Carnahan.

### 1. Procedure

The apparatus is assembled according to Fig. 3. *A* is a 500-cc. Pyrex filter flask. *B* is a 2-l. three-neck round-bottom flask; into one of the side necks is fitted a 300-cc. dropping fun-

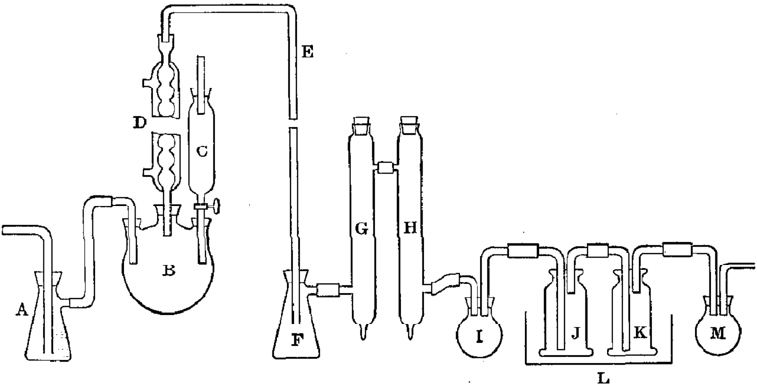



Fig. 3.

nel *C* (Note 1), and the second side neck is closed with a loose-fitting, well-greased rubber stopper, which serves as a safety valve against any sudden increase of pressure in the generator. A long (75-cm.) water-cooled bulb condenser *D* is connected to

* Apparatus for the reaction described in Org. Syn. **4**, 27.

the middle neck of the generator flask *B*. The large bore glass tube *E* connects the top of the condenser *D* with trap *F*, a 500-cc. filter flask, which is connected by means of a short rubber tube to the drying towers *G* and *H* (Note 2). These towers are conveniently made from glass condenser jackets; the bottom ends are sealed and the top ends closed with rubber stoppers (Note 3). Tower *H* is connected to " sight flask " *I*, a 500-cc. round-bottom flask. This in turn is connected to the absorption vessels *J* and *K* (500-cc. gas washing bottles), which are immersed in an ice-salt bath contained in dish *L*. Absorption bottle *K* is connected to " sight flask " *M*, a 500-cc. round-bottom flask similar to *I*. By means of the sight flasks *I* and *M* the efficiency of absorption can be judged by the depth of color. Flask *I* also serves to catch any liquid sucked back from the absorption vessels.

Before finally assembling the apparatus, the various units are charged as follows: *A* is one-third filled with water to serve as a bubble counter. Generator *B* is about one-quarter filled with dry arsenious oxide, pea size or powdered. Drying towers *G* and *H* are filled with anhydrous calcium chloride. (It is well to place a wad of glass wool in front of the entrance and exit tubes.) In each of the two absorption bottles *J* and *K* is placed 200 g. of ethyl malonate. Dish *L* is filled with an ice-salt freezing mixture.

When assembled as indicated, the apparatus is ready for operation. Concentrated nitric acid is run, in small portions, into generator *B* from dropping funnel *C*. After the action has started, the nitric acid must be forced into flask *B* by applying a small air pressure at the top of dropping funnel *C* and then opening the stopcock. Later on, when the gas generation slackens, flask *B* is heated with a smoky flame. The evolution of gas is maintained at a steady rate by increasing the heat until finally all the arsenious oxide has dissolved and the frothing has ceased. During the whole operation a slow stream of compressed air (Note 4) is passed through the apparatus from " bubble counter " *A*. The stream of air is insufficient if any colorless gas, which turns brown on coming in contact with the air, leaves the apparatus at *M*. When the arsenious oxide is exhausted, as shown

by a slackening in gas evolution, the old generator is removed and a fresh one put in its place. (If the generator is first allowed to cool somewhat, this change can be accomplished without much discomfort.) The moist oxides of nitrogen, in passing up through the condenser *D*, lose most of their moisture and the gas on passing down through tube *E* should deposit very little water in trap *F*. The gas is then thoroughly dried in the towers *G* and *H*. When the calcium chloride in *G* becomes wet (after several runs) the tower is refilled; at the same time *G* and *H* are interchanged. After passing through the drying towers and through flask *I*, the gas is absorbed by the cold ethyl malonate in vessels *J* and *K*. The ethyl malonate becomes dark green in color. There should be an increase in weight of about 200 g. in absorption bottle *J* in two or three hours (Note 5).

The rest of the directions are the same as in the original article by Dox (Note 6).

## 2. Notes

1. All the stoppers in this apparatus are of rubber, well greased with vaseline.

2. All rubber connections of this apparatus must be of thick tubing, well greased inside.

3. Ordinary gas-drying towers may also be used for *G* and *H*.

4. The reaction between arsenious oxide and concentrated nitric acid yields a mixture of nitric oxide and nitrogen dioxide. It also contains some nitrogen tetroxide and perhaps trioxide, the amount in equilibrium depending upon the temperature of the gas. The compressed air forced in via flask *A* insures an excess of oxygen, and thus complete oxidation. Only a slow stream is necessary, two to three bubbles per second.

5. A complete run should if possible be made without stopping. However, if the preparation must be stopped before completion, the absorption vessels should be disconnected, weighed, and protected against moisture by calcium chloride tubes. They lose weight on standing owing to decomposition of the intermediate compound.

6. Upon adding the calculated amount of water to ethyl oxomalonate, decolorization takes place immediately with evolution of heat, and on cooling a solid mass of ethyl dihydroxymalonate results. After recrystallization from chloroform the product melts at 56–57°. (Communicated by Elizabeth Gilman and T. B. Johnson.)

7. This work was assisted by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

# XVI

## GLUTARIC ACID

$$CH_2O + 2CH_2(CO_2C_2H_5)_2 \xrightarrow{(C_2H_5)_2NH} CH_2[CH(CO_2C_2H_5)_2]_2 + H_2O$$

$$CH_2[CH(CO_2C_2H_5)_2]_2 + 4H_2O \rightarrow$$
$$CH_2(CH_2CO_2H)_2 + 4C_2H_5OH + 2CO_2$$

Submitted by T. J. Otterbacher.
Checked by F. C. Whitmore and F. L. Carnahan.

### 1. Procedure

*Ethyl Propane-α,α,γ,γ-tetracarboxylate.*—To a mixture of 1600 g. (10 moles, 1510 cc.) of ethyl malonate (Note 1) and 400 g. of 40 per cent formalin (5.3 moles) in a 5-l. round-bottom flask, cooled to 5° by immersion in ice, is added 25 g. (35 cc.) of diethylamine. The mixture is then allowed to come to room temperature and remain for fifteen hours, after which the flask is heated under a reflux condenser on a boiling water bath for six hours. The aqueous layer is then separated, and the residue is distilled under reduced pressure (Note 2) from a 3-l. special Claisen flask (Org. Syn. **1**, 40). The ester distils at 190–200°/12 mm.(210–215°/20 mm.) The yield (Note 3) is 1000 g. (61 per cent of the theoretical amount).

*Glutaric Acid.*—A mixture of 125 g. (0.37 mole) of the above product, 125 cc. of concentrated hydrochloric acid and 125 cc. of water is heated (Note 4) in a 1-l. flask under a reflux condenser until it becomes homogeneous (six to eight hours). The contents of the flask are then evaporated to dryness, and the residual glutaric acid is transferred to a 100-cc. Claisen flask and distilled under diminished pressure. The fraction boiling at 185–195°/10 mm. is collected. It is moistened with water (Note 5) and heated gently, after which it is dried at 30°. On recrystallization from

benzene, it separates in colorless needles, m.p. 96–97°. The yield is 38–40 g. (76–80 per cent of the theoretical amount).

## 2. Notes

1. The ethyl malonate used was a fraction of the technical grade boiling over a 3° range under diminished pressure.

2. The ester is distilled slowly at first in order to vaporize the water at a temperature below 50°.

3. The high boiling residue (500 g.) is stated[1] to contain considerable amounts of ethyl pentanehexacarboxylate.

4. In order to prevent loss of material through the condenser by bumping, the flask should be heated in an oil bath at 115° or its contents stirred vigorously.

5. The product is moistened to convert any anhydride, formed at the high temperature of distillation, into the acid.

## 3. Methods of Preparation

The preparation of glutaric acid by the hydrolysis of trimethylene cyanide has been described in a previous article in this series,[2] which includes a bibliography of the literature. The present method is a modification of that of Knoevenagel.[3]

[1] Gault, Bull. soc. chim. (4) **11**, 380 (1912).

[2] Marvel and Tuley, Org. Syn. **5**, 69 (1925).

[3] Knoevenagel, Ber. **27**, 2346 (1894).

## XVII

# HEPTANOL-2

$$CH_3CO(CH_2)_4CH_3 \xrightarrow{Na + C_2H_5OH} CH_3CH(OH)(CH_2)_4CH_3$$

Submitted by F. C. WHITMORE and T. OTTERBACHER.
Checked by HENRY GILMAN and H. J. HARWOOD.

### 1. Procedure

IN a 3 l. round bottom flask, fitted with an efficient Liebig condenser (100 × 1 cm.), 228 g. (2 moles) of methyl *n*-amyl ketone (Org. Syn. 7, 60) is dissolved in a mixture of 600 cc. of 95 per cent alcohol and 200 cc. of water. One hundred and thirty grams (5.4 moles) of sodium in the form of wire is gradually added through the condenser. During the addition of the sodium the flask is cooled with running water (Note 1) so that the reaction does not become unduly violent (Note 2).

When the sodium has dissolved (Note 3), 2 l. of water is added and the mixture is cooled to 15°. The upper oily layer is then separated, washed successively with a mixture of 25 cc. of concentrated hydrochloric acid and 25 cc. of water and with water alone, dried over 20 g. of anhydrous sodium sulfate, and distilled with a fractionating column (Note 4). After a small forerun of low-boiling liquid, the pure heptanol distils at 155–157.5°. The yield is 145–150 g. (62–65 per cent of the theoretical amount).

### 2. Notes

1. If no cooling is used, condensation products are formed and the yield of heptanol is reduced considerably.

2. The temperature can be held conveniently below 30° by cooling with ice. Such cooling when accompanied by stirring is

particularly helpful during the early addition of the sodium (either as wire or in small pieces). With cooling and stirring, very little refluxing takes place and after the addition of about 60 g. of sodium the reaction slows down to such an extent that large amounts of sodium can be added at once without danger of excessive heating.

3. The time required for addition of the sodium may be significantly decreased by the use of mechanical stirring. Although the yield is not increased appreciably by stirring, frothing is prevented and for this reason the sodium may be added more rapidly. If the sodium fails to dissolve readily at the end of the reaction, more water may be added to the mixture.

4. The submitters used a Young column with 20 disks 3 cm. apart. The checkers used a Glinsky 3-bulb column.

### 3. Methods of Preparation

Heptanol-2 has been prepared by the action of *n*-amyl magnesium bromide on acetaldehyde,[1] and by the reduction of methyl *n*-amyl ketone in alcoholic solution by means of sodium.[2]

[1] Henry, Rec. trav. chim. **28**, 446 (1909).

[2] Thoms and Mannich, *Ber.* **36**, 2544 (1903); Pickard and Kenyon, J. Chem. Soc. **99**, 58 (1911).

## XVIII

## LAURYL ALCOHOL

$$C_{11}H_{23}CO_2C_2H_5 \xrightarrow{Na+C_2H_5OH} C_{11}H_{23}CH_2OH$$

Submitted by S. G. Ford and C. S. Marvel.
Checked by F. C. Whitmore and D. J. Loder.

### 1. Procedure

The central neck of a 5-l. three-neck round-bottom flask is fitted with a stopper carrying a mercury-seal mechanical stirrer. One of the side necks is connected by means of a short piece of heavy rubber tubing to a large reflux condenser about 2 m. long, with an inner tube 2.5 cm. in diameter (Note 1). The third neck is fitted with a separatory funnel.

In the flask are placed 70 g. (3 moles) of sodium and 200 cc. of dry toluene (Note 2). The flask is heated in an oil bath until the sodium is melted. The stirrer is then started and, when the sodium is finely divided, the oil bath is removed and the mixture allowed to cool. Stirring must be continued during the cooling in order to keep the sodium finely divided.

When the mixture has cooled to about 60°, there are added from the separatory funnel, first, a solution of 114 g. (0.5 mole) of ethyl laurate (Note 3) in 150 cc. of absolute alcohol (Note 4), then 500 cc. more of alcohol, as rapidly as is possible (Note 5) without loss of material through the condenser. The time required for the addition of the ester solution and the alcohol is less than five minutes, usually two or three minutes. When the reaction has subsided, the flask is heated on a steam bath until the sodium is completely dissolved (Note 6). The mixture is then steam distilled to remove the toluene and ethyl alcohol.

The contents of the flask are transferred to a separatory funnel while still hot and washed three times with 200-cc. portions of hot water to remove the sodium laurate (Note 7). The lauryl alcohol is extracted with ether from the cooled mixture and the washings. The combined ether extracts are washed with water, sodium carbonate solution, and again with water, and dried over anhydrous magnesium sulfate. The ether is evaporated and the lauryl alcohol distilled under diminished pressure. The yield is 60–70 g. (65–75 per cent of the theoretical amount) of a product boiling at 143–146°/18 mm. or 198–200°/135 mm. (Note 8).

## 2. Notes

1. The reaction is very vigorous, and unless the condenser has a wide bore finely divided sodium may be forced out the top and bad fires may result. The inner tube of the condenser may advantageously be made of brass or copper.

2. The toluene is dried by distillation; the first 10 per cent is discarded and the remainder is stored over sodium until used.

3. The ethyl laurate used was prepared by the alcoholysis of cocoanut oil and fractionation of the resulting esters. The material boiled at 127–132°/5 mm.

4. The grade of the absolute alcohol used in the reduction is very important. Alcohol dried over lime gives very poor yields. In these experiments the alcohol used was dried with magnesium methylate (Org. Syn. **7**, 37).

5. The best yields are obtained when the reductions are carried out rapidly. If the reaction seems to be about to get out of control, the stirrer is stopped and the mixture is cooled with an ice pack.

6. If several reductions are being made, time will be saved by transferring the mixture at this point to another flask, thus having the original apparatus ready for another reduction.

7. Unless the sodium laurate is carefully removed, it causes troublesome emulsions.

8. Ethyl undecylenate has been reduced to undecylenyl alcohol (b.p. 123–125°/6 mm.) in 70 per cent yields; ethyl myristate

to myristyl alcohol (b.p. 170–173°/20 mm.; m.p. 39–39.5°) in 70–80 per cent yields; ethyl palmitate to cetyl alcohol (b.p. 178–182°/12 mm.; m.p. 48.5–49.5°) in 70–78 per cent yields by using this same procedure.

### 3. Methods of Preparation

Lauryl alcohol has been prepared by the reduction of the aldehyde with zinc dust and acetic acid;[1] by the reduction of esters of lauric acid with sodium and absolute alcohol[2] or with sodium, liquid ammonia, and absolute alcohol;[3] by the reduction of lauramide with sodium and amyl alcohol.[4] The method in the above procedure is essentially that described by Levene and Allen.[5]

[1] Krafft, Ber. **16**, 1718 (1883).

[2] Bouveault and Blanc, Bull. soc. chim. (3) **31**, 674 (1904); Ger. pat. 164,294 [Frdl. **8**, 1260 (1905)]; Levene and Allen, J. Biol. Chem. **27**, 443 (1916); Marvel and Tanenbaum, J. Am. Chem. Soc. **44**, 2649 (1922); Adams and Marvel, Org. Chem. Reagents, Univ. of Ill. Bull., Vol. 20, No. 8, p. 54 (1922).

[3] Chablay, Compt. rend. **156**, 1021 (1913); Ann. chim. (9) **8**, 215 (1917).

[4] Scheuble and Loeble, Monatsh. **25**, 348 (1904).

[5] Levene and Allen, J. Biol. Chem. **27**, 443 (1916).

XIX

## MALONONITRILE

$$CNCH_2CONH_2 + PCl_5 \rightarrow CH_2(CN)_2 + POCl_3 + 2HCl$$
$$2CNCH_2CONH_2 + POCl_3 \rightarrow 2CH_2(CN)_2 + HPO_3 + 3HCl$$

Submitted by B. B. Corson, R. W. Scott and C. E. Vose.
Checked by C. S. Marvel and J. Harmon.

### 1. Procedure

One hundred and fifty grams (1.8 moles) of pure cyanoacetamide (Org. Syn **9**, 36) is thoroughly mixed in a large (20-cm.) mortar with 150 g. (0.7 mole) of phosphorus pentachloride (Notes 1, 2 and 3). This mixture is transferred (Note 4) as quickly as possible to a 500-cc. Claisen flask equipped with a 360° thermometer and an air-intake tube (Note 5). The Claisen is connected by means of a double-length air condenser to a 250-cc. filter flask which in turn is connected to a water pump (Note 6) through a manometer.

After the system has been evacuated to about 30 mm. of mercury, the Claisen flask is immersed in a boiling water bath. The mixture melts and its color deepens to orange. Boiling commences (in about fifteen minutes) before the solid is completely melted and the pressure rises to about 150 mm., owing to the liberation of hydrogen chloride and phosphorus oxychloride (Note 7). When the evolution of gas has slackened, as indicated by the fall of pressure and the less vigorous boiling of the reaction mixture (thirty to thirty-five minutes), the receiver is changed. The distilling flask is removed from the boiling water bath, wiped dry, and immersed in an oil bath at 140° (Notes 8 and 9); the fresh receiver is placed in ice water

The malononitrile begins to distil at 113°/30 mm. (125°/50

mm.). The temperature of the oil bath is slowly raised over a period of twenty-five minutes to 180° (Note 10) and the nitrile collected between 113° and 125°. When the distillation has almost ceased, the oil bath is removed so as to prevent discoloration of the product (Note 11). The yield (Note 12) of crude nitrile is 80–95 g. (67–80 per cent of the theoretical amount). The nitrile may be purified by vacuum distillation (Note 13) with about 10 per cent loss; it is collected between 113° and 120°/30 mm. One distillation yields a water-clear liquid, which quickly freezes to an ice-like solid (Note 14) melting at 28–30°. The product has a faint odor resembling that of acetamide.

## 2. Notes

1. The phosphorus pentachloride should be of good quality —a dry solid.

2. The weights of the reactants correspond to the ratio of 5 molecules of amide to 2 molecules of pentachloride. The use of larger proportions of phosphorus pentachloride leads to lower yields.[3]

3. Phosphorus pentoxide has been used as dehydrating agent but the pentachloride method is much superior. With the pentoxide method there is always trouble due to the formation of a black, sticky mass which swells up during the latter part of the experiment and often disrupts the apparatus.

4. This transfer is greatly facilitated by the use of a 15-cm. (6-inch) glass funnel whose stem has been cut off and the hole enlarged to almost the size of the neck of the Claisen flask. The mixture is emptied into the body of the funnel and pushed through the large hole by means of a glass rod. Particular care should be exercised, for any considerable breathing of the fumes brings on a harsh cough which may last for several days. A gas mask should be worn.

5. To avoid plugging, the air-intake tube is not drawn out to a capillary.

6. An oil pump cannot be used because of the corrosive acid fumes.

7. Unless the phosphorus oxychloride is to be recovered, it is advisable to allow it to be carried away by the suction. This is easily accomplished if the receiver is not cooled.

8. If the initial temperature of the oil bath is below 140°, the nitrile distils too slowly (with consequent lowering of yield); if the temperature is above 140°, the nitrile comes over too fast. In the latter case, some nitrile condenses in the rubber tubes leading to the pump, thus clogging the line.

9. The flask should be immersed as far as possible in the oil (to within about 100 mm. of the top of the flask). This is important. A 1-gal. enamel-ware coffee-pot makes an excellent oil bath. An ordinary soldered vessel will not stand the temperature.

10. The temperature of the oil bath must not rise much above 180°, else the distillate becomes colored and violent bumping is apt to occur. The distillate should not be allowed to solidify in the condenser. This is most apt to occur during the first part of the distillation. The solid is easily melted by heating with a small flame.

11. The residue in the Claisen flask can be softened by water and broken up with a rod. The small amount remaining is easily removed with concentrated nitric or, preferably, concentrated sulfuric acid.

12. The keynote to success in this preparation is speed. Malononitrile is a sensitive substance and it must be removed from the reaction mixture as rapidly as possible. After experience with one or two runs the yields will consistently be better than 67 per cent.

13. Malononitrile can be distilled in small amounts (50 cc. or so) at ordinary pressure; the boiling point is around 220°. However, the longer heating necessary with larger amounts is apt to cause violent decomposition. In such a case the liquid darkens, boils spontaneously, and finally spurts from the flask in a cloud of white fumes and burning liquid; the latter partially solidifies to a brittle red solid.

14. Nitrogen determination indicates a purity of 99.5 per cent. The product remains colorless for at least one year if

stored in brown bottles protected from the light. If kept in ordinary bottles and exposed to the light, the nitrile quickly darkens.

15. This work was aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

### 3. Methods of Preparation

Malononitrile has been prepared by the action of phosphorus pentoxide on malonamide[1] and on cyanoacetamide;[2] the above method is based upon that of Hesse.[3]

[1] Henry, Compt. rend. **102**, 1394 (1886).
[2] Henry, Compt. rend. **102**, 1395 (1886).
[3] Hesse, Am. Chem. J. **18**, 726 (1896).

XX

## METHYL OXALATE

$$(CO_2H)_2 + 2CH_3OH \xrightarrow{H_2SO_4} (CO_2CH_3)_2$$

Submitted by EVERETT BOWDEN.
Checked by C. S. MARVEL and A. T. KOIDE.

### 1. Procedure

IN a 500-cc. Pyrex flask, fitted with a cork which loosely carries a glass mechanical stirrer and a separatory funnel, are placed 90 g. (1 mole) of anhydrous oxalic acid (Org. Syn. 1, 67; 10, 78) and 100 cc. of methanol (Note 1). Then while the mixture is rapidly stirred, 35 cc. of pure concentrated sulfuric acid (Note 2) is slowly added through the separatory funnel. The mixture is heated, if necessary (Note 3), nearly to boiling, then filtered as rapidly as possible through a 15-cm. filter paper placed in a slightly heated glass funnel, the filtrate being collected in a 500-cc. wide-mouth Erlenmeyer flask. The first flask is rinsed out with 40 cc. of hot methanol, which is poured through the filter paper. After twenty-four hours (Note 4) (at 15°) the crystals are filtered off with suction, sucked as dry as possible, pressed between filter paper and air-dried for a few minutes. The filtrate after cooling to about −10° is filtered rapidly, and the product dried as before. A total of 100–115 g. of material, slightly moist with sulfuric acid and melting at 50–52°, is obtained.

To recrystallize, the above product is dissolved in 100 cc. of redistilled methanol, filtered through a warm funnel and allowed to crystallize. After several hours the crystals are filtered off, and the filtrate treated as before. A total of 80–90 g. (68–76

per cent of the theoretical amount) of methyl oxalate, melting at 52.5–53.5° (Note 5), is obtained.

## 2. Notes

1. The methanol used is the commercial (almost acetone-free) grade known as Columbian Spirits. This material is redistilled for recrystallizing the methyl oxalate.

2. Less sulfuric acid than that employed gives a smaller yield, whereas larger quantities sometimes result in a product that gives difficulty in filtration. It is essential that the acid be added slowly and with vigorous stirring to prevent local superheating and darkening of the solution and product. Some commercial grades of methanol become quite dark in contact with sulfuric acid. The grade of methanol used here does not discolor, the filtrates being only light yellow.

3. Solution of the oxalic acid causes a sharp drop in temperature whereas solution of the sulfuric acid raises the temperature.

4. The major portion of the reaction is complete within a few minutes, but several hours are necessary for complete crystallization.

5. Larger batches give the same percentage yield as the one described. When several batches are to be run, the alcohol from the first recrystallization becomes the starting alcohol for the second batch, etc. This increases the yield somewhat.

## 3. Methods of Preparation

Methyl oxalate has been prepared by distilling a mixture of oxalic acid, methyl alcohol and sulfuric acid;[1] by dissolving anhydrous oxalic acid in hot methyl alcohol;[2] by esterifying oxalic acid with methyl alcohol, using anhydrous hydrogen

[1] Dumas and Peligot, Ann. chim. phys. (2) **58**, 44 (1835); Ann. **15**, 32 (1835); Nohler, Ann. **81**, 376 (1852).

[2] Erlenmeyer, Jahresb. **1874**, 572.

chloride as a catalyst;[3] by methanolysis of ethyl oxalate;[4] by passing vapors of dry methanol through hydrated oxalic acid until the water has been removed;[5] by a process in which the methyl alcohol-water mixture evolved from hydrated oxalic acid and methanol is dried over potassium carbonate and returned to the reaction flask.[6] The method described in the procedure is simpler than any of these and gives very satisfactory yields.

[3] Rising and Stieglitz, J. Am. Chem. Soc. **40**, 726 (1918).

[4] Pfannl, Monatsh. **31**, 316 (1914); Reimer and Dounes, J. Am. Chem. Soc. **43**, 950 (1921).

[5] Dutt, J. Chem. Soc. **123**, 2714 (1923).

[6] Kenyon, Org. Syn. **5**, 60 (1925).

XXI

## *m*-NITROACETOPHENONE

$$C_6H_5COCH_3 + HNO_3 \longrightarrow m\text{-}NO_2C_6H_4COCH_3 + H_2O$$

Submitted by B. B. CORSON and R. K. HAZEN.
Checked by ROGER ADAMS and W. W. MOYER.

### 1. Procedure

In a 1-l. wide-mouth Erlenmeyer flask, immersed in an ice-salt bath contained in a 2-gal. earthenware crock, is placed 150 cc. of concentrated sulfuric acid. The flask is equipped with an efficient mechanical stirrer, a small dropping funnel and a thermometer reaching almost to the bottom of the flask (Note 1). The stirrer is started, and when the sulfuric acid has cooled to ice temperature or below, 59 cc. (0.5 mole) of pure acetophenone is slowly dropped in from the dropping funnel at such a rate (about ten minutes for the addition) that the temperature does not rise above 5° (Note 2). After the reaction mixture has cooled, this time to about −7°, the cooled (15–20°) nitrating mixture, consisting of 40 cc. (0.65 mole) of nitric acid (sp. gr. 1.42 at 15.5°) (Note 3) and 60 cc. of concentrated sulfuric acid, is added through the dropping funnel at such a rate (100–120 drops per minute) that the temperature of the reaction mixture remains at 0° or lower (Note 4). After the nitrating acid has been added, stirring is continued for ten minutes longer and the contents of the flask are poured (Note 5) with vigorous manual stirring, into a mixture of 750 g. of cracked ice and 1500 cc. of water. The product separates as a yellow flocculent solid.

After the ice has melted, the product is filtered by suction and the somewhat sticky mass pressed as dry as possible. It is transferred to a mortar and triturated with three successive 300-cc. portions of cold water (to remove acid); it is then stirred to a mush with two successive 25-cc. portions of ice-cold ethyl

alcohol (to remove adhering oil); the solid is pressed dry on the suction filter after each of the five washings. The product is pressed on a porous plate, and when fairly dry (about one hour) is dissolved in 100–120 cc. of hot ethyl alcohol (Note 6). The dark solution is filtered quickly through a small suction funnel (Note 7) and the hot filtrate is poured slowly into 1000 cc. of cold water which is stirred vigorously (Note 8) with a stirring rod during the addition and for several minutes afterward. After standing a few minutes the yellow solid is filtered off by suction, washed with 200 cc. of cold water, sucked dry and pressed out on a porous clay plate.

When the reprecipitated *m*-nitroacetophenone (50–55 g.) is dry it is dissolved in 100 cc. of hot alcohol in a 300-cc. Erlenmeyer flask. The flask is then immersed in an ice bath and shaken vigorously while crystallization is taking place. Because of the great change in solubility between 60° and 50° the agitation of the liquid must be vigorous during this temperature interval, or large clumps of crystals will be formed instead of the purer and more easily dried mush. After the temperature has reached 20° (about one hour) the mixture is filtered by suction (Note 9). The solid (Note 10) is washed with 10 cc. of ice-cold alcohol and pressed dry on a clay plate. The product is light yellow; it softens at 74° and melts at 76–78°. The total yield is 45 g. (55 per cent of the theoretical amount).

## 2. Notes

1. The only flask found suitable for this preparation is the 1-l. wide-mouth Erlenmeyer. A large flask is necessary to insure rapid cooling. A propeller with long, wide blades agitates the viscous liquid much more efficiently than a stirrer of the centrifugal type. The blades should be as long as allowed by the wide mouth of the flask. The thermometer which is to record the temperature of the reaction mixture should enter at an angle and reach almost to the bottom of the flask, since the amount of liquid is small. The thermometer should have the zero point at least 15 cm. from the bulb in order to facilitate reading of the temperature. It is essential that the temperature

be watched throughout the experiment. A smaller ice-salt bath than that contained in a 2-gal. earthenware crock is inadequate.

2. The same dropping funnel can be used, without washing, for the addition of the concentrated sulfuric acid, the acetophenone and the nitrating mixture. With rapid stirring the acetophenone can be easily added in seven minutes without raising the temperature of the reaction mixture above 3°.

3. Nitric acid of lower specific gravity than 1.42 at 15.5° yields an impure product. Ordinary concentrated nitric acid usually has to be strengthened by the addition of fuming nitric acid.

4. Two conditions are necessary for a good nitration: low temperature (0° or below) and rapidity of addition of the nitrating mixture (not longer than forty-five minutes). With efficient cooling the temperature can be held between −5 and 0°. If the temperature should rise once or twice to 3° no harm is done provided the reaction mixture is quickly cooled back to the correct temperature. In order to avoid local heating the delivery tube of the dropping funnel should be so directed as to deliver the nitrating acid near the site of greatest agitation.

The rate of stirring must be rapid. The optimum speed will be different for different stirrers, depending on the shape and size of the blades. For the stirrer described the speed is 1600 r. p. m. During the addition of acetophenone this high speed is not necessary; in fact, it cannot be maintained on account of excessive splashing. However, during the addition of the nitrating acid the reaction mixture thickens and high-speed stirring becomes possible. The ice-salt mixture must be stirred repeatedly with a stick, and fresh ice and salt must be added from time to time. The temperature of the bath should be around −16°. Enough liquid should be present in the cooling bath so that the lower half of the flask is immersed in brine. If no especial care is exercised, the addition of the nitrating acid requires from two to three hours in order to maintain the temperature at 0° or below. This long exposure to the mixture of sulfuric and nitric acids is as harmful as a rise of temperature; the product is of poor quality and the yield drops from 55 to 15 per cent or less.

5. The experiment should not be stopped until the product has been poured into ice water.

6. Although 55° suffices to dissolve the *m*-nitroacetophenone it is desirable to bring the alcoholic solution to a boil to avoid crystallization during filtration.

7. Excessive frothing in the filter flask is easily checked by pinching off the suction tube from time to time.

8. Vigorous stirring and slow pouring are absolutely necessary. In the absence of either, the product will separate in a lumpy rather than in the flocculent form.

9. Since the solubility curve is so flat in the vicinity of room temperature it is not necessary to cool very low before filtering. The difference between 20° and 10° amounts to only 1 g. per 100 cc. of solution. The solubility of *m*-nitroacetophenone in 96 per cent alcohol is as follows:

| Temperature | Weight in 10 cc. | Temperature | Weight in 10 cc. |
|---|---|---|---|
| 8° | 0.16 | 48° | 1.88 |
| 17 | 0.25 | 50 | 2.38 |
| 22 | 0.31 | 52 | 3.08 |
| 23 | 0.34 | 53.5 | 4.05 |
| 27 | 0.41 | 56 | 5.46 |
| 28 | 0.45 | 57 | 8.05 |
| 32 | 0.64 | 59 | 11.00 |
| 39 | 0.97 | 60 | 15.60 |
| 42 | 1.22 | | |

10. A small additional yield (about 5 g.) may be obtained from the mother liquor by concentrating to 20 cc. and then cooling in ice.

11. This work was aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

### 3. Methods of Preparation

*m*-Nitroacetophenone has usually been prepared by the nitration of acetophenone;[1] it has also been made by the hydrolysis of *m*-nitrobenzoylacetoacetic ester.[2]

[1] Engler and Emmerling, Ber. **3**, 886 (1870); Buchka, Ber. **10**, 1714 (1877); Engler, Ber. **18**, 2238 (1885); v. Kostanecki and Tambor, Ber. **84**, 1691 (1901); Rupe, Braun and Lembrzuski, Ber. **34**, 3522 (1901).

[2] Gevekoht, Ann. **221**, 334 (1884).

XXII

# OXALIC ACID (ANHYDROUS)

$$C_2H_2O_4 \cdot 2H_2O \rightarrow C_2H_2O_4 + 2H_2O$$

Submitted by EVERETT BOWDEN.
Checked by C. S. MARVEL and E. H. WOODRUFF.

## 1. Procedure

A LABORATORY oven (Note 1) is equipped with as many clay plates or enameled pie plates or trays as it will accommodate and is adjusted to operate at 98–99° (Notes 2 and 3). When the temperature has become constant the plates are removed, rapidly covered with a layer (not over 3–4 mm. deep) of pulverized (Note 4) hydrated oxalic acid, and then quickly replaced in the oven. The temperature will drop slightly for a few minutes (Note 5). After the oven has regained the temperature for which it was adjusted, it is heated for two hours longer at this temperature. The product is then removed, crushed if slightly caked, and quickly bottled. The yield from 100 g. of hydrated oxalic acid is 69–70 g. (96–98 per cent of the theoretical amount) (Note 6). The product is 99.5–100 per cent pure, as indicated by titration with standard alkali.

## 2. Notes

1. Any type of oven may be used, but the automatic electric requires least attention. As many trays may be used as there are shelves in the oven. The trays are heated with the oven to decrease the subsequent first drop in temperature.

2. Some *slight* sublimation is always noticed, and the acid tends to cake. At higher temperatures heavy losses are caused by sublimation, and the caked material is very imperfectly dehydrated; there is also some darkening. Under the conditions given a white product is formed.

3. The dehydration is faster at higher temperatures. Numerous experiments showed that one hour and twenty minutes at a temperature of 113-115° gave a nearly theoretical yield of slightly colored material containing 97 per cent of oxalic acid. A one-hour heating at the same temperature gave a " yield " of 102 per cent containing 94 per cent of oxalic acid. This result applies to a C. P. starting material; technical acid gives somewhat less favorable results.

4. The acid should be powdered so that 50 per cent will pass a 60-mesh sieve and all will pass a 40-mesh sieve. A 9-inch plate can be used for about 50 to 100 g. of acid.

5. The oven temperature always drops a few degrees, owing to the cooling effect of the cold acid and the evaporation of a relatively large quantity of water. This drop in temperature is much less noticeable in a large oven than in a small one, and in one having thermostatic control in contrast to manual control.

6. The amount of material which may be dried will depend entirely on the size of the oven and the size and number of trays used. By repeating the runs several kilograms of material may be dried in a day with very little attention.

7. The success of this method of dehydration depends upon an exact control of all conditions specified.

### 3. Methods of Preparation

Oxalic acid is readily dehydrated by the use of carbon tetrachloride,[1] but this method has the disadvantage of complexity, relative slowness, and the use of relatively large quantities of carbon tetrachloride.

Most methods depend upon the direct removal of water from oxalic acid crystals by the application of heat.[2] The weakness of this lies chiefly in a lack of standardization.

[1] Hultman, Davis and Clarke, J. Am. Chem. Soc. **43**, 368 (1921); Clarke and Davis, Org. Syn. **1**, 67 (1921).

[2] Rising and Stieglitz, J. Am. Chem. Soc. **40**, 726 (1918); Orndorff, Lab. Manual of Org. Chem., 67 (1922); Kenyon, Org. Syn. **5**, 59 (1925).

XXIII

## α-PHENYL-β-BENZOYLPROPIONITRILE

$$C_6H_5CH{=}CHCOC_6H_5 + HCN \rightarrow C_6H_5CH(CN)CH_2COC_6H_5$$

Submitted by C. F. H. ALLEN and R. K. KIMBALL.
Checked by J. B. CONANT and HELEN O'BRIEN.

### 1. Procedure

THE following preparation, through the filtration of the crude solid and washing with water, should be carried out in a hood with a good draft.

Into a 5-l. flask or bottle set in a water bath and fitted with a stirrer, thermometer, and separatory funnel, are placed 208 g. (1 mole) of benzalacetophenone (Note 1), 3.5 l. of 95 per cent ethyl alcohol (Note 2), and 60 g. (1 mole) (Note 3) of glacial acetic acid (Note 3). The mixture is warmed with stirring to 35°, and a solution of 130 g. (2 moles) of potassium cyanide in 375 cc. of water is added from the separatory funnel over a period of about fifteen minutes. The initial greenish color changes to yellow after the acetic acid has all reacted and the solution has become alkaline (Note 3). Stirring is continued for three hours, the temperature being maintained at 35°. During this time about half of the nitrile crystallizes. The flask is then loosely stoppered and left in a cool place for about fifty hours (conveniently out-of-doors in cold weather, but out of direct sunlight), after which the solid is filtered off and washed, first with 500 cc. of cold 50 per cent alcohol, and then with water until free from potassium cyanide (silver nitrate test). The yield of air-dried material melting at 125° is 220–227 g. (93–96 per cent of the theoretical amount). This product is sufficiently pure for most purposes, although it contains traces of a high-melting substance. If a product of higher melting point is

desired, it may be recrystallized from 1 l. of 95 per cent alcohol or 375 cc. of acetone. Pure phenylbenzoylpropionitrile melts at 127°.

## 2. Notes

1. Crude alkali-free, air-dried benzalacetophenone is used (Org. Syn. 2, 1).

2. The preparation may be carried out in a more concentrated solution (1000 cc. of alcohol) with the same yield, but an inferior product is obtained. If this is done, it is best to stir for fifteen minutes at 50° after all the cyanide has been added and then cool in tap water. Since the product separates as an oil from a solution of this concentration, it is best to inoculate with a crystal of the nitrile.

3. If the solution becomes too alkaline, the nitrile formed will add to a second molecule of unsaturated ketone so readily that the product will consist almost entirely of a high-melting (284–286°) substance. For this reason it is essential to measure the acetic acid accurately; if too much is used, addition of hydrocyanic acid will not take place.

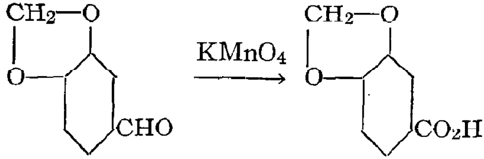
## 3. Methods of Preparation

$\alpha$-Phenyl-$\beta$-benzoylpropionitrile has been prepared by the action of sodium or potassium cyanide on $\beta$-chlorobenzylacetophenone,[1] and by the addition of hydrocyanic acid in the presence of sodium or potassium cyanide to benzalacetophenone.[2]

[1] Anschütz and Montfort, Ann. **284**, 2 (1895); Rupe and Schneider, Ber. **28**, 960 (1895).

[2] Hann and Lapworth, J. Chem. Soc. **85**, 1358 (1904); Lapworth and Wechsler, J. Chem. Soc. **97**, 41 (1910).

# PIPERONYLIC ACID



Submitted by R. L. SHRINER and E. C. KLEIDERER.
Checked by H. T. CLARKE and S. GRAFF.

## 1. Procedure

SIXTY grams (0.4 mole) of piperonal (Note 1) and 1500 cc. of water are placed in a 5-l. flask fitted with an efficient mechanical stirrer. The flask is placed on a steam bath and heated to 70–80° and the stirrer started. A solution of 90 g. of potassium permanganate in 1800 cc. of water is allowed to flow (Note 2) into the emulsion of piperonal and water (Note 3) over a period of forty to forty-five minutes. The stirring and heating are continued for an hour longer, at the end of which time the permanganate is reduced. A sufficient quantity of 10 per cent potassium hydroxide solution is added to make the solution alkaline. The mixture is filtered while hot and the manganese dioxide is washed with three 200-cc. portions of hot water. The combined filtrate and washings are cooled. At this point any unreacted piperonal that separates out must be filtered off (Note 4). The solution is now acidified with hydrochloric acid, the acid being added until no further precipitate forms. The resulting piperonylic acid is filtered off, washed with cold water until free of chlorides, and dried. The yield is 60–64 g. (90–96 per cent of the theoretical amount) of a colorless product melting at 224–225° (corr.). For most purposes the crude material is

pure enough, but it may be crystallized from ten times its weight of 95 per cent ethyl alcohol, yielding 52–56 g. (78–84 per cent of the theoretical amount) of needles melting at 227–228° (corr.).

## 2. Notes

1. The commercial grade of piperonal, m.p. 36°, may be used without purification.

2. The reverse order of addition lowers the yield to 50 per cent.

3. Vigorous mechanical stirring is necessary in order to emulsify the molten piperonal thoroughly with the water.

4. If the temperature of the reaction mixture is kept between 70° and 80° and the permanganate is added at the rate stated, the piperonal will be entirely oxidized.

## 3. Methods of Preparation

Piperonylic acid has been made by the oxidation of piperic acid,[1] piperonal,[1] safrole[2] and isosafrole[2] with potassium permanganate. It has also been prepared by the action of methylene iodide on protocatechuic acid[3] in the presence of alkali.

[1] Fittig and Mielck, Ann. **152**, 40 (1869).

[2] Ciamician and Silber, Ber. **23**, 1160 (1890).

[3] Fittig and Remsen, Ann. **168**, 94 (1873).

# XXV

## *l*-PROPYLENE GLYCOL

$$CH_3COCH_2OH + 2H \xrightarrow{\text{(Reductase of yeast)}} CH_3CHOHCH_2OH$$

Submitted by P. A. Levene and A. Walti.
Checked by F. C. Whitmore and J. Pauline Hollingshead.

### 1. Procedure

A solution of 1 kg. of sucrose in 9 l. of water is placed in a 20-l. bottle provided with a gas trap. A paste of baker's yeast (Note 1) is made by breaking up 1 kg. of yeast and gradually stirring in 1 l. of water. This is then added to the sugar solution and the mixture is allowed to stand at room temperature until a lively evolution of gas starts (from one to three hours). To the vigorously fermenting solution 100 g. of freshly prepared acetol (p. 1) is added, and the mixture is allowed to stand at room temperature until the reaction subsides (Note 2). The bottle is then transferred to an incubator at 32°, when the fermentation recommences. At the end of three days the reaction is generally completed, and the solution when tested with Fehling's reagent gives a negligible test for reducing sugars.

At this point 20–30 g. of short glass fiber or asbestos is added and the yeast is filtered out by suction. The filtrate is concentrated to a thick syrup under diminished pressure on a water bath, care being taken to keep the temperature below 40° (Note 3). The residue (about 200 cc.) is taken up in a mixture of 400 cc. of absolute alcohol and 100 cc. of dry ether (Note 4). The precipitate formed is removed by centrifuging, the supernatant liquid is decanted, and the residue is extracted with a mixture of 200 cc. of 98.5 per cent alcohol and 100 cc. of dry

ether (Note 5). The combined alcohol-ether solutions are concentrated under diminished pressure at 35–40° to a thick syrup. The residue is again taken up in a mixture of 400 cc. of 98.5 per cent alcohol and 100 cc. of dry ether and centrifuged (Note 5). The supernatant liquid is concentrated under diminished pressure and distilled from a modified Claisen flask (Org. Syn. 1, 40). The yield of the crude product boiling at 86–91°/12 mm. is approximately 100 g. The crude material is refractionated and collected at 88–90°/12 mm. or 187–189°/760 mm. The final product (Note 4) is a colorless liquid having a density 1.04 and specific rotation $[\alpha]_D^{20} = -15.0°$. The yield is 50–60 g. (49–58 per cent of the theoretical amount) (Note 6).

## 2. Notes

1. Fleischmann's yeast is satisfactory.

2. The addition of the acetol may cause the reaction to slacken for a time.

3. The evaporation must be carried out at as low a temperature as is practicable. A suitable device for vacuum evaporation of large volumes of liquid is given in Org. Syn. 4, 54.

4. The product reacts slightly acid. If an entirely neutral *l*-propylene glycol is desired, the syrup first obtained should be made neutral with a solution of sodium methylate in methyl alcohol, and again concentrated and extracted as indicated.

5. If a centrifuge is not available, about 15 g. of short glass fiber or asbestos may be added to the solution, stirred with a mechanical stirrer for five minutes or thoroughly shaken, and filtered on a suction filter with similar results to those obtained by centrifuging.

6. The optically active glycols are a convenient starting material for the preparation of optically active carbinols, hydroxy-acids, etc. The biological method of asymmetric reduction is perhaps the only convenient method for the preparation of these glycols. The steps in the preparation of other optically active glycols are identical with those of *l*-propylene glycol. In some cases it is found convenient to oxidize the chlorohydrin to the

corresponding chloroketone—the subsequent steps remaining the same as given above.

### 3. Methods of Preparation

*l*-Propylene glycol has been obtained from the optically inactive glycol by the action of bacteria,[1] and by means of strychnine compounds.[2] The present method is based on that of Färber, Nord and Neuberg.[3]

[1] LeBel, Jahresb. **1881**, 512.
[2] Grün, Ber. **52B**, 260 (1919).
[3] Färber, Nord, and Neuberg, Biochem. Z. **112**, 313 (1920).

# XXVI

## *iso*-PROPYL LACTATE

$$CH_3CHOHCO_2H + (CH_3)_2CHOH \rightarrow CH_3CHOHCO_2CH(CH_3)_2 + H_2O$$

Submitted by F. A. McDermott.
Checked by C. R. Noller.

### 1. Procedure

In a 3-l. round-bottom flask (Note 1) fitted with a 1-meter fractionating column[1] are placed 450 g. of anhydrous *iso*-propyl alcohol (Note 2), 212 g. (2 moles) of U. S. P. 85 per cent lactic acid, 1 l. of benzene, and 5 cc. of concentrated sulfuric acid. The flask is placed in an air bath on an electric hot plate (Note 3) and heated until the benzene-*iso*-propyl alcohol-water ternary mixture distils over at 66.5°. Distillation is continued slowly (six to seven hours) until the temperature at the head of the column rises to and persists at 71–72° (*iso*-propyl alcohol-benzene binary), and no further separation of water occurs. Ten grams of precipitated calcium carbonate is then added to the mixture, and distillation is continued until the temperature rises to 80° in order to remove most of the benzene and excess of *iso*-propyl alcohol (Notes 4 and 5). The contents of the flask are then filtered into a modified Claisen distilling flask (Org. Syn. **1**, 40) and the filtrate is distilled under reduced pressure. Cuts are taken to 60°, 60–75°, 75–80°, and 80–100° at 32 mm. The fraction boiling at 75–80°/32 mm. is *iso*-propyl lactate and weighs 130–160 g. By redistilling the high and low fractions an additional 30–60 g. is obtained, bringing the total yield to 160–180 g. (60–68 per cent of the theoretical amount). The ester may be redistilled at atmospheric pressure (with some loss due to decomposition) at 166–168°.

## 2. Notes

1. In large charges it is well to employ a two-neck flask, using the spare neck for introducing the calcium carbonate later in the process.

2. *Iso*-propyl alcohol is very difficult to dry satisfactorily. The water binary mixture, boiling at 80.35°, contains 12.1 per cent of water by weight. The ternary mixture with benzene, boiling at 66.5°, contains 73.8 per cent benzene, 18.7 per cent *iso*-propyl alcohol and 7.5 per cent water. Hence by adding 120 g. of dry benzene to 100 g. of the *iso*-propyl-water binary, and distilling off until the temperature reaches 82°, there will remain 55 to 60 g. of nearly dry *iso*-propyl alcohol. The commercial anhydrous alcohol was used in this preparation.

3. A water or steam bath or oil bath may be used.

4. The temperature of the vapors should not be allowed to rise above 72° before the addition of the calcium carbonate. If too much alcohol is removed before the acid is neutralized, charring and resinification take place with a decrease in the yield of ester.

5. The recovered benzene and excess *iso*-propyl alcohol may be dried by distillation and used in a subsequent run.

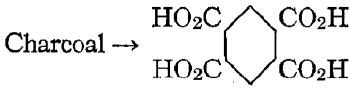
## 3. Methods of Preparation

*Iso*-propyl lactate has been prepared by heating *iso*-propyl alcohol and lactic acid in a sealed tube at 170°,[2] and from silver lactate and *iso*-propyl iodide, together with the *iso*-propyl ester of α-*iso*-propoxy-propionic acid.[3] Direct esterification of the acid with the alcohol, with sulfuric acid, has failed to give a yield greater than 20 per cent of the theoretical amount, and the product has been less pure.

[1] Clarke and Rahrs, Ind. Eng. Chem. **15**, 349 (1923).
[2] Silva, Bull. soc. chim. (2) **17**, 97 (1872).
[3] Purdie and Lander, J. Chem. Soc. **73**, 298 (1898).

## XXVII

## PYROMELLITIC ACID



Submitted by E. PHILIPPI and R. THELEN.
Checked by H. T. CLARKE and S. GRAFF.

### 1. Procedure

IN a 5-l. round-bottom flask set on a wire gauze in a hood, and provided with a thermometer, are placed 100 g. of finely powdered pine or spruce charcoal (Note 1) and 650 cc. of 82–88 per cent sulfuric acid (sp. gr. 1.76–1.80) (Note 2) and a small drop of mercury (Note 3). The mixture is heated with a small flame and the temperature is raised to 250° during four hours. During another half hour the temperature is raised to 290°, when the acid begins to volatilize, and the mixture to froth and expand greatly (Note 4). During the next hour the temperature is raised to 300° and then to 315° during the following hour. Meanwhile the mixture has thickened somewhat. Then much bubbling and spurting take place and fine white needles of pyromellitic anhydride begin to collect in the neck of the flask (Note 5). Fifty cubic centimeters of sulfuric acid is now added, the walls of the flask being rinsed with it; after again being heated to 250° for a few minutes, the syrupy liquid is transferred to a 1000-cc. tubulated retort while still hot (Note 6). The flask is rinsed with the minimum amount of water and the washings are added to the retort. The water is first distilled off, then 30 g. of acid potassium sulfate is added to the mixture and the latter is heated vigorously with a free flame. At first almost colorless sulfuric acid distils. As soon as crystals of pyromellitic anhy-

dride appear, the receiver is replaced by one containing 50 cc. of water. The distillation is continued until nothing more passes over. At this point most of the pyromellitic anhydride has collected in the neck of the retort (Note 7). The retort is rinsed out with 100 cc. of water and the washings are filtered and evaporated on the steam bath to about 25 cc. The last distillate is also evaporated to 25 cc. On cooling, pyromellitic acid crystallizes. The product from both portions is collected on a suction funnel, using hardened filter paper, washed with two 10-cc. portions of ice water (Note 8) and recrystallized from four parts of boiling water. After drying at 105° the product (containing 2 moles of water of crystallization) melts at 271° (262° uncorr.). The yield is 6–8 g. (Note 9).

## 2. Notes

1. The yield of pyromellitic acid depends considerably on *the kind of charcoal used. An experiment with ordinary willow* charcoal gave none of the desired product.

2. The specific gravity of the acid used should not vary from the limits indicated.

3. A series of experiments has proved the helpful action of mercuric sulfate.

4. If the time for the first stage (temperature below 250°) is shortened, the frothing is greater at this point, and the final yield is lowered.

5. The end of the reaction can be readily detected by the bubbling and spurting which take the place of the quiet boiling. If the mixture is not fairly thick, less sulfuric acid should be used in the next run. If it is solid, more acid should be used.

6. The transfer to the retort must be made before the mixture solidifies. The best method of closing the tubulure of the retort (unless this consists of Pyrex glass) is by means of a glass stopper too small for the hole and wrapped with asbestos paper moistened with sodium silicate solution.

7. If considerable amounts of pyromellitic anhydride separate in the neck of the retort, it is advisable to rinse it into a

clean dish rather than into the receiver, which contains considerable sulfuric acid.

8. In recovering pyromellitic acid from the mother liquor it is advisable first to remove the sulfuric acid by adding a slight excess of barium hydroxide and acidifying to Congo red with hydrochloric acid.

9. The anhydride of pyromellitic acid may be obtained from the dry anhydrous acid by boiling with acetic anhydride.

### 3. Method of Preparation

Pyromellitic acid may be obtained by the oxidation of benzene derivatives containing organic substituents in the 1,2,4,5 positions: by the oxidation of durene with nitric acid;[1] by condensing benzene with diethyl malonyl chloride, reducing to the hydrocarbon, again condensing in the same way, and finally oxidizing the resulting tetraethyl benzodihydrindenedione;[2] and by an analogous synthesis from *m*-xylene, involving condensation with acetyl chloride, reduction and oxidation.[3]

Mellitic acid can be decarboxylated to yield pyromellitic acid, either by the action of heat alone[4] or in the presence of sulfuric acid.[5]

The oxidation of wood charcoal by means of sulfuric acid leads to mellitic acid and its decarboxylation products;[6] nitric acid may also be employed.[7] Pyromellitic acid has also been obtained by the electrolytic oxidation of graphite in an alkaline medium.[8]

[1] Jacobsen, Ber. **17**, 2516 (1884).

[2] Freund, Fleischer and Gofferjé, Ann. **414**, 26 (1918).

[3] Philippi, Seka and Froeschl, Ann. **428**, 300 (1922).

[4] Erdmann, Ann. **80**, 281 (1851); Baeyer, Ann. Suppl. **7**, 36 (1870).

[5] Erdmann, Ann. **80**, 282 (1851); Silberrad, J. Chem. Soc. **89**, 1795 (1906).

[6] Verneuil, Compt. rend. **118**, 195 (1894); **132**, 1340 (1901); Philippi and Thelen, Ann. **428**, 296 (1922).

[7] Silberrad, Ger. pat. 214,252, Frdl. **9**, 173 (1911); Philippi and Rie, Ann. **428**, 287 (1922).

[8] Bartoli and Papasogli, Gazz. chim. ital. **12**, 113 (1882); **13**, 37 (1883).

XXVIII

## β-RESORCYLIC ACID

$$m\text{-}C_6H_4(OH)_2 \xrightarrow{CO_2 + KHCO_3} 1,2,4\text{-}C_6H_3(CO_2H)(OH)_2$$

Submitted by M. NIERENSTEIN and D. A. CLIBBENS.
Checked by ROGER ADAMS and F. E. KENDALL.

### 1. Procedure

IN a 5-l. flask fitted with a reflux condenser a solution containing 200 g. (1.8 moles) of resorcinol, 1000 g. (9.9 moles) of potassium acid carbonate (Note 1) and 2 l. of water (Note 2) is heated slowly on a steam bath for four hours. The flask is then placed over a flame and refluxed vigorously for thirty minutes; a rapid stream of carbon dioxide is passed through the solution during this heating process.

While still hot the solution is acidified by adding 900 cc. of concentrated hydrochloric acid (sp. gr. 1.19) from a separatory funnel with a tube delivering the acid to the bottom of the flask to prevent the formation of a layer of acid over the unneutralized solution. The flask is allowed to cool to room temperature and is then chilled in an ice-bath. The resorcylic acid crystallizes out in prisms, giving an almost colorless product which upon exposure to the air turns pink, owing to contamination with a small amount of resorcinol. The yield of crude acid is 225 g. By extracting the mother liquor with ether several times, 35 g. of resorcylic acid and some unchanged resorcinol can be recovered. The resorcylic acid is extracted from the ether by shaking with an aqueous solution of sodium bicarbonate. The aqueous solution is acidified with hydrochloric acid and again extracted with ether. The ether is then evaporated, leaving the resorcylic

acid, which is usually highly colored and must be recrystallized several times from boiling water and charcoal to remove the color.

The combined yield of crude acid (260–270 g.) is dissolved in 1 l. of water, boiled with about 25 g. of Norite, filtered through a heated filter, and crystallized by placing in an ice-salt freezing mixture and stirring vigorously. A finely crystalline, colorless product is obtained in this way. If it is allowed to crystallize slowly the crystals are somewhat colored. The yield of pure resorcylic acid melting at 216–217° is 160 170 g. (57–60 per cent of the theoretical amount) (Note 3).

## 2. Notes

1. Instead of potassium acid carbonate, the sodium salt in corresponding quantity may be used.

2. If less than ten parts of water to one of resorcinol is used, the yield is diminished.

3. The air-dried crystals lose at 110° a quantity of water corresponding to a half mole of water of crystallization.

## 3. Methods of Preparation

This method[1] of preparing β-resorcylic acid is a modification of the method given by Bistrzycki and Kostanecki.[2]

[1] Clibbens and Nierenstein, J. Chem. Soc. **107**, 1494 (1915).

[2] Bistrzycki and Kostanecki, Ber. **18**, 1984 (1885).

## XXIX

## SODIUM 2-BROMOETHANESULFONATE

$$BrCH_2CH_2Br + Na_2SO_3 \rightarrow BrCH_2CH_2SO_3Na + NaBr$$

Submitted by C. S. Marvel and M. S. Sparberg.
Checked by F. C. Whitmore and D. J. Loder.

### 1. Procedure

In a 5-l. round-bottom flask fitted with a reflux condenser, a mechanical stirrer, and a separatory funnel are placed 615 g. (3.27 moles) of ethylene dibromide (Note 1), 1250 cc. of 95 per cent alcohol and 450 cc. of water (Note 2). The stirrer is started and the mixture heated to boiling. To the well-stirred boiling mixture a solution of 125 g. (1 mole) of sodium sulfite (anhydrous salt) in 450 cc. of water is added through the separatory funnel over a period of about two hours. The solution is boiled under a reflux condenser for two hours after all of the sulfite solution has been added; the condenser is then set for distillation and the alcohol and the ethylene bromide are distilled (Note 3). The remaining water solution is poured into a large evaporating dish and evaporated to dryness on the water bath. The sodium 2-bromoethanesulfonate is extracted from the sodium bromide and unchanged sodium sulfite with 2 l. of boiling 95 per cent alcohol. On cooling the solution, most of the salt crystallizes and the mother liquor is used for a second extraction of the residue. The yield is 165–190 g. (78–90 per cent of the theoretical amount). The product (Note 4) may be further purified by recrystallizing from alcohol and drying in an oven at 110° (Note 5). The recovery on recrystallization is 75–80 per cent.

## 2. Notes

1. The large excess of ethylene dibromide is necessary to reduce the formation of the disulfonic acid.

2. The concentration of the alcohol seems to be important and poorer yields were obtained when it was changed in either direction.

3. By diluting the alcoholic distillate from the reaction mixture with 10 l. of water, it is possible to recover about 400 g. of ethylene dibromide.

4. This product may contain as much as 2 to 5 per cent of sodium bromide, but it is pure enough for the preparation of taurine (p. 98). A very pure product can be obtained by a second crystallization from alcohol.

5. The salt is slightly hygroscopic.

## 3. Methods of Preparation

The directions given in the procedure are based on those of Kohler.[1] No other practical method of preparation has appeared in the literature.

[1] Kohler, Am. Chem. J. **20**, 692 (1898); Marvel, Bailey and Sparberg, J. Am. Chem. Soc. **49**, 1836 (1927).

## XXX

## TAURINE

(2-Aminoethanesulfonic Acid)

$$BrCH_2CH_2SO_3Na + NH_3 \rightarrow NH_2CH_2CH_2SO_3H + NaBr$$

Submitted by C. S. Marvel and C. F. Bailey.
Checked by F. C. Whitmore and D. J. Loder.

### 1. Procedure

A solution of 110 g. (0.52 mole) of sodium 2-bromoethanesulfonate (p. 96) in about 2 l. (28 moles) of concentrated aqueous ammonia (sp. gr. 0.9) is allowed to stand for five to seven days (Note 1) and is then evaporated to dryness. The last of the water is removed by heating on a steam bath. The residue is dissolved in the minimum quantity of hot water (about 500 cc.) and, if necessary, treated with 5 g. of decolorizing carbon (Norite). The colorless solution is concentrated to 65–70 cc., and 250 cc. of 95 per cent alcohol is added. In a short time taurine mixed with some sodium bromide separates. When crystallization is complete, the crude taurine is collected on a filter and recrystallized by dissolving in 100 cc. of hot water and then adding to the solution enough 95 per cent ethyl alcohol (about 500 cc.) to give a final concentration of 80 per cent of alcohol. The taurine which separates is usually free from bromides. However, occasional runs have to be recrystallized four or five times to remove all of the sodium bromide. The yield of pure taurine (Note 2) is 31–36 g. (48–55 per cent of the theoretical amount).

### 2. Notes

1. The reaction is about 25 per cent complete in five hours, 60 per cent complete in thirty hours, and 90 per cent complete in five days, as indicated by titration of the bromide ion.

2. The purity of the taurine prepared by this method was established by analysis.

### 3. Methods of Preparation

Taurine is generally prepared from ox bile[1] or the large muscle of the abalone.[2] It has been synthesized from isethionic acid through chloroethanesulfonic acid followed by the action of aqueous ammonia;[3] from ethyleneimine and sulfur dioxide;[4] from 2-mercaptothiazoline by oxidation with bromine water;[5] from bromoethylamine and ammonium sulfite;[6] and from acetaldehyde by a complex set of reactions involving sulfonation, formation of the aldehyde ammonia and the imido sulfonic acid and finally reduction.[7] The method given in the procedure has recently appeared in the literature.[8]

[1] Hammersten, Z. physiol. Chem. **32**, 456 (1901); Tauber, Beitr. Phys. Path. **4**, 324 (1904).

[2] Schmidt and Watson, J. Biol. Chem. **33**, 499 (1918).

[3] Kolbe, Ann. **122**, 42 (1862); Anschütz, Ann. **415**, 97 (1918).

[4] Gabriel, Ber. **21**, 2667 (1888).

[5] Gabriel, Ber. **22**, 1153 (1889).

[6] Reychler, Bull. soc. chim. Belg. **32**, 247 (1923).

[7] Auzies, Revue générale de chimie pure et appl. **14**, 278 [Chem. Zentr. **1911**, II, 1433].

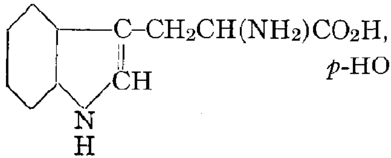
[8] Marvel, Bailey and Sparberg, J. Am. Chem. Soc. **49**, 1836 (1927).

# XXXI

## *l*-TRYPTOPHANE

(By-product, *l*-Tyrosine)

Digestion of Casein →




$p$-$HOC_6H_4CH_2CH(NH_2)CO_2H$

Submitted by GERALD J. COX and HARRIETTE KING.
Checked by H. T. CLARKE and JESSICA P. LELAND.

### 1. Procedure

*Tryptophane.*—In an 8-l. (2-gal.) bottle is placed 600 g. of commercial casein (coarse powder), which is then covered with about 3200 cc. of tap water at 37° (Note 1). The bottle is shaken until all of the casein is moistened. A solution of 60 g. of anhydrous sodium carbonate (Note 2) and 6 g. of sodium fluoride (Note 3) in 1 l. of water at 37° is added. A thin paste of 20 g. of commercial pancreatin in 100 cc. of water (37°) is poured in. The mixture is covered with a layer of toluene (80 cc.), diluted to 6 l., stoppered, shaken thoroughly, and placed in a warm room or bath at 37°.

After four or five days, with daily shakings, most of the casein is in solution and chalky masses of tyrosine begin to separate. After five days, a second dose of 20 g. of pancreatin in 100 cc. of water is added. After twelve days, the bottle is cooled in an ice-box over night and the undissolved material is filtered off (Note 4) and reserved for the preparation of tyrosine.

The filtrate (6900–7000 cc.) is measured into a 16-l. (4-gal.) stone jar and for every liter there is added 163 cc. of dilute sulfuric

acid (1 vol. of 95 per cent sulfuric acid and 1 vol. of water, cooled to room temperature). The first part of the acid must be added cautiously on account of the liberation of carbon dioxide.

The tryptophane is precipitated by adding a solution of 200 g. of mercuric sulfate (Note 5) in a mixture of 1860 cc. of water and 140 cc. of concentrated (95 per cent) sulfuric acid. After standing for twenty-four to forty-eight hours, the clear liquid is siphoned out and the yellow precipitate is filtered off and washed (Note 6) with a solution of 100 cc. of concentrated sulfuric acid in 1900 cc. of distilled water containing 20 g. mercuric sulfate, until the filtrate is colorless and Millon's test is atypical (Note 7); about 1500 cc. is necessary. The precipitate is washed with three successive 500-cc. portions of distilled water to remove most of the sulfuric acid.

The moist precipitate (120–130 g.) is suspended with mechanical stirring in 1200–1300 cc. of distilled water, and a hot, 20 per cent aqueous solution of barium hydroxide is added until the mixture is permanently alkaline to phenolphthalein (about 120 cc. is required). A rapid stream of hydrogen sulfide is passed in with stirring until the mercury is completely precipitated (Note 8). The precipitate is filtered off and washed with water until a sample of the washings gives a negative test for tryptophane with bromine water (Note 9). The barium is removed from the combined filtrate and washings by adding the exact amount of dilute sulfuric acid (Note 10) and filtering. The filtrate is concentrated under reduced pressure to about 80 cc.

The tryptophane is extracted from the aqueous solution by repeatedly shaking in a separatory funnel with 25-cc. quantities of *n*-butyl alcohol; water is added from time to time to keep the volume approximately constant (Note 11). The butyl alcohol extract is distilled under reduced pressure. After the water present has distilled over, the tryptophane precipitates in the distilling flask and may cause bumping. When all water has been removed, as is indicated by non-formation of drops on the side of the condenser, the distillation is stopped, and, after cooling, the tryptophane is filtered off and washed with a little fresh butyl alcohol. Such extractions and distillations are con-

tinued until the quantities of tryptophane obtained are negligibly small (Note 11).

The tryptophane so produced (7–8 g.) varies somewhat in quality in different runs. It is purified by recrystallization from 60 cc. of dilute alcohol (2 vol. of 95 per cent alcohol to 1 vol. of water), filtering off from the hot solution an appreciable quantity of insoluble matter and subjecting this to a second extraction with a further 10-cc. quantity of aqueous alcohol. The solution is decolorized by the addition of 1 g. of decolorizing carbon (Norite) and allowed to stand in the ice-box; the silvery leaflets of tryptophane are filtered off and washed successively with cold 70 per cent, 80 per cent, 95 per cent alcohol and finally with a little ether. Less than half the tryptophane is obtained in each crystallization (Note 12). The yield of pure (Note 13) tryptophane is 4.0–4.1 g., together with under 0.1 g. of less pure product.

*Tyrosine.*—The insoluble material (160–170 g.) obtained on filtering the digestion mixture is suspended in 320 cc. of water and 80 cc. of concentrated (36 per cent) hydrochloric acid, and the mixture boiled gently for thirty minutes (Note 14). After straining through cheese-cloth, decolorizing with 6 g. of Norite (Note 15) and filtering hot (Note 16), the warm (60–70°) solution is shaken with three 20-cc. portions of benzene (Note 17), and heated to boiling (Note 18). A slight excess (120–150 cc.) of 28 per cent ammonia is cautiously added, and the mixture is allowed to stand over night in the ice-box. The crystalline product is then filtered off and washed with three 40-cc. portions of ice-water. After drying, it weighs about 23 g. The mother liquor and washings are evaporated to about 200 cc., when a second crop is obtained, weighing slightly under 1 g.

The combined product is suspended in 400 cc. of water and dissolved by adding 8 g. of sodium hydroxide in 20–30 cc. of water (Note 19); 2 g. of Norite is added, and the solution filtered. The residue is washed on the funnel with 20–30 cc. of hot distilled water. The filtrate is heated to boiling (Note 18) and treated with 13 cc. of hydrochloric acid (Note 20), when crystallization usually begins. The mixture is then acidified to litmus with acetic acid (Note 21) and allowed to stand over night in the

refrigerator. The resulting tyrosine is filtered off and washed with ice-cold distilled water (130–150 cc. is necessary) until the washings are free of chloride. The product is dried in air or in a vacuum oven. The yield is 17.0–18.2 g. of pure white, silky needles of tyrosine. A second crop (about 0.5 g.) of a slightly less pure product may be obtained on concentrating the mother liquor to about 120 cc.

## 2. Notes

1. Tryptic action is more rapid if all water used is at 37°. Distilled water is not necessary at this stage.

2. This is a considerable excess of sodium carbonate. Smaller quantities might be satisfactory.

3. The sodium fluoride probably inhibits the action of the oxidases.

4. This filtration may be slow. Büchner funnels of 20-cm. diameter are best used; the preparation is allowed to suck dry from a single filling and the filter paper then changed.

5. Approximately this quantity of mercuric sulfate is necessary to precipitate the tryptophane completely, as judged by the Hopkins-Cole glyoxylic acid test.

6. This washing is to remove tyrosine, which is precipitated as a mercury compound somewhat more soluble than the tryptophane precipitate. The mercuric sulfate addition tends to reduce the tryptophane solubility.

7. A persistent red color is always obtained in the filtrates but the final color is distinctly different from that due to tyrosine.

8. Excess hydrogen sulfide must remain in the solution after standing. A sample of the filtrate, after acidifying with acetic acid, should give a copious black precipitate with lead acetate.

9. The bromine water test is somewhat more satisfactory for pure tryptophane than the glyoxylic acid test. Hydrogen sulfide may interfere (owing to sulfur formation) and must be boiled out first. The solution to be tested must be acid with acetic acid.

10. This amount is best determined in a 20-cc. aliquot sample, employing 2 per cent sulfuric acid in a burette.

11. In checking, it was found satisfactory to extract in a continuous apparatus (Fig. 4). Extraction is continued until the liquid in the flask begins to bump on account of the separation of solid; a new charge of butyl alcohol is then employed, about five charges being necessary. This process is repeated until the residue after a three-hour period of extraction fails to give the red color, characteristic of tryptophane, with bromine water. The time necessary will of course depend upon the rate of boiling; in checking, it was found to be twenty-eight to thirty hours.

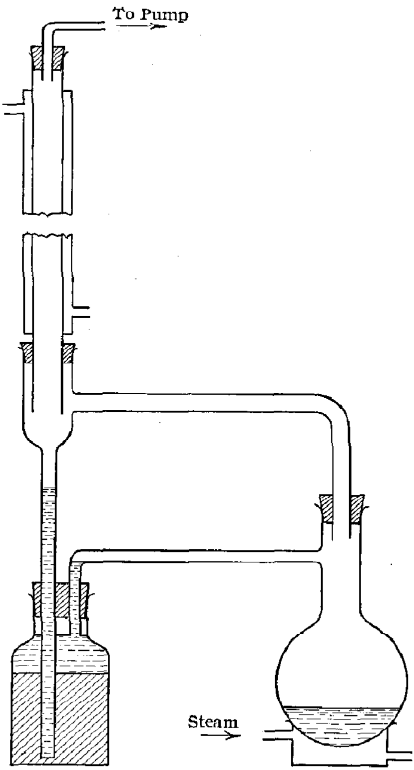



FIG. 4.

12. The recrystallization of the crude tryptophane is an extremely troublesome process. Not only must a less soluble by-product be removed, but the mother liquors contain a more soluble, gummy impurity in considerable proportion. After collecting each crop, the mother liquor must be evaporated to a small volume on the steam bath and treated with a double volume of alcohol. This process is repeated until no further crystals are obtained, but only a gum.

13. The purity of the tryptophane has been checked by the optical rotation ($[\alpha]_D = -28$ to $-33°$) and by analysis for amino nitrogen (6.8–6.9 per cent) by Van Slyke's method.

14. The boiling acid solution hydrolyzes protein material that otherwise greatly retards filtration.

15. The Norite used in this preparation is insufficient to decolorize the solutions completely, but gives a white final product.

16. All the filtrations in the purification of tyrosine, except possibly the last, are best done on a 20-cm. Büchner funnel. Whenever charcoal is used, kieselguhr may be employed to obtain a clear filtrate.

17. Benzene extracts traces of substances, probably fatty acid, that retard filtration and greatly alter the quality of the final product.

18. The tyrosine crystallizes in long, silky needles, easy to filter, if the solution is neutralized at the boiling point.

19. A small amount of flocculent impurity remains undissolved.

20. The hydrochloric acid is added to provide chloride ion as an index of complete washing.

21. Tyrosine is very slightly soluble in all concentrations of acetic acid. Therefore any excess of acetic acid does not redissolve the tyrosine.

## 3. Methods of Preparation

The above procedure for preparing tryptophane is an adaptation from the methods of Hopkins and Cole,[1] Dakin,[2] and Onslow.[3]

Tyrosine, as a primary product, may be readily prepared by hydrolyzing silk with hydrochloric acid, neutralizing the acid with sodium hydroxide, and finally acidifying with acetic acid.

[1] Hopkins and Cole, J. Physiol. **27**, 418 (1902).

[2] Dakin, Biochem. J. **12**, 302 (1918).

[3] Onslow, Biochem. J. **15**, 392 (1921).

# APPENDIX

## LATER REFERENCES TO PREPARATIONS IN PRECEDING VOLUMES

(The following references are to methods of possible preparative value that have been recently described. The numbers in parentheses following the name of a compound refer to the volume and page of Organic Syntheses.)

**Acetal** (3, 1):

(*a*) By the action of acetylene on alcohol in the presence of a mercury salt. Consortium f. elektrochem. Ind. Ges., Brit. pats. 257,622 and 264,791 (1925, 1926). [C. A. **21**, 3057 (1927); **22**, 243 (1928).]

(*b*) A study of the mechanism of the reaction. Adkins and Broderick, J. Am. Chem. Soc. **50**, 178 (1928).

**Acrolein** (6, 1):

By the action of heat on glycerol, using a "bleaching earth" catalyst such as "frankonite." Freund, U. S. pat. 1,672,378 (1928). [C. A. **22**, 2571 (1928).]

**Adipic acid** (5, 9):

By oxidizing cyclohexanol with nitric acid containing ammonium vanadate. Deutsche Hydrierwerke A. G., Ger. pat. 473,960 (1926). [C. A. **23**, 2988 (1929).]

*dl*-**Alanine** (9, 4):

By shaking a solution of ammonia and ammonium pyruvate with colloidal palladium in the presence of hydrogen, employing starch paste to stabilize the colloid. Aubel and Bourguel, Compt. rend. **186**, 1844 (1928).

**Allyl alcohol** (1, 15):

A study of the mechanism of the thermal decomposition of glyceryl formates; detailed directions for improved yields are

supplied. Delaby and Dubois, Compt. rend. **187**, 949 (1928); **188**, 710 (1929).

**Arsonoacetic acid** (4, 5):

By the action of chloroacetic acid on sodium arsenite; isolated and purified through the lead salt. Romberg and Ohman, Svensk. Kem. Tids. **36**, 119 (1924). [C. A. **19**, 36 (1925).]

**Benzil** (1, 25; 6, 6):

By oxidizing benzoin in methyl alcoholic sodium methoxide solution by the addition of iodine. Corson and McAllister, J. Am. Chem. Soc. **51**, 2822 (1929).

**Benzoic anhydride** (3, 21):

(*a*) On treating benzoic acid with acetic anhydride at room temperature no mixed anhydride is formed, but benzoic anhydride separates with acetic anhydride of crystallization. van der Haar, Rec. trav. chim. **47**, 321 (1928).

(*b*) By treating benzotrichloride at 100–115° with water in the presence of certain heavy metal salts. Brit. Dyestuffs Corp., Ltd., Payman and Hall, Brit. pat. 280,373 (1926). [C. A. **22**, 2951 (1928).]

**Benzoin** (1, 33):

By the reduction of benzoic acid by means of magnesium and magnesium iodide. Gomberg and Bachmann, J. Am. Chem. Soc. **50**, 2762 (1928).

**Benzophenone** (8, 26):

(*a*) *o*-Benzoylbenzoic acid is heated with a small amount of its copper salt at 260°. Dougherty, J. Am. Chem. Soc. **50**, 571 (1928).

(*b*) By the action of carbon dioxide upon phenylmagnesium bromide. Ivanoff, Bull. soc. chim. (4) **43**, 441 (1928).

**Benzyl benzoate** (2, 5):

(*a*) Benzaldehyde is treated with aluminium ethoxide or butoxide, preferably in solution in an ester, such as an ethyl or butyl ester corresponding to the catalyst, or the molten catalyst

may be added to the benzaldehyde, the temperature allowed to rise, and the product distilled in vacuo. MATHESON, Brit. pat. 270,651 (1926). [C. A. **22**, 1597 (1928).]

(*b*) Benzaldehyde is treated with iodomagnesium butoxide in ether. The condensation runs to 45 per cent completion in five days. The product contains about 10 per cent of benzyl ether. GRIGNARD and FLUCHAIRE, Ann. chim. **9**, 19 (1928).

***n*-Butyl *n*-butyrate** (5, 23):

By the action of aluminium butoxide on butyraldehyde. SKIRROW, Can. pat. 279,974 (1928). [C. A. **22**, 2756 (1928).]

***n*-Butyl chloride** (5, 27):

By the action of hydrogen chloride on butyl alcohol under pressure at temperatures above 130° in silver or silver-lined vessels. BASEL and KAUFLER, Ger. pat. 462,993 (1928). [C. A. **22**, 4133 (1928).]

***n*-Butylmalonic ester (ethyl)** (4, 11):

The importance of using dry alcohol is emphasized. BHIDE and SUDBOROUGH, J. Indian Inst. Sci. A, **8**, 89 (1925). [Chem. Zentr. **1926**, I, 81.]

**Catechol** (3, 27):

(*a*) By treatment of a solution of phenol in sulfuric acid with sodium peroxide. MAGIDSON, POROZOVSKA and SELIGSOHN, Trans. Sci. Chem. Pharm. Inst. (Moscow) **6**, 23 (1923). [C. A. **22**, 3884 (1928).]

(*b*) By heating cellulose waste from wood, straw, etc. with alkaline solutions under pressure. MELANDER and WALLIN, Swed. pat. 62,831 (1927). [C. A. **21**, 4069 (1927).]

***o*-Chlorotoluene** (3, 33):

(*a*) By a modification of the Sandmeyer reaction. BRYD, Roczniki Chem. **7**, 436 (1927). [C. A. **22**, 2372 (1928).]

(*b*) Separation of the *o*- and *p*-isomers by selective sulfonation of the *o*- derivative at 90–120° for two to three hours. WAHL, U. S. pat. 1,596,325 (1926). [C. A. **20**, 3299 (1926).]

**Cupferron** (4, 19):

The addition of 0.05 g. of acetophenetidide to 100 cc. of cupferron reagent tends to prevent decomposition of the latter. GERMUTH, Chemist–Analyst **17**, no. 3, 3, 15 (1928). [C. A. **22**, 3372 (1928).]

**Cyclopentanone** (5, 37):

Similar to the method in Organic Syntheses, but barium oxide is used instead of barium hydroxide. VAVON and APCHIE, Bull. soc. chim. (4) **43**, 667 (1928).

*l*-**Cystine** (5, 39):

By the hydrolysis of hair or completely defatted wool, followed by exact adjustment of the *p*H to 4.8. OKABE, J. Biochem. (Japan) **8**, 441 (1928).

**Diacetone alcohol** (1, 45):

By the action of potassium hydroxide or other suitable alkali upon acetone in benzene solution. The benzene represents a liquid miscible with the acetone, but not with the condensing agent. THOMSON, U. S. pat. 1,654,103 (1927). [C. A. **22**, 787 (1928).]

**Diallyl cyanamide** (5, 43):

The procedure described in Organic Syntheses. VLIET, U. S. pat. 1,659,793 (1928). [C. A. **22**, 1365 (1928).]

**Di-*p*-tolylethane** (4, 23):

By the reduction of $\alpha,\alpha$-di-*p*-tolylethylene with sodium in absolute alcohol. ANSCHÜTZ and HILBERT, Ber. **57**, 1699 (1924).

**Ethyl *p*-aminobenzoate** (8, 66):

By oxidation of acet-*p*-toluidide, followed by esterification of the *p*-aminobenzoic acid. CHEMNITIUS, Pharm. Zentralh. **68**, 765 (1927).

**Ethyl oxomalonate** (4, 27):

(*a*) Considerable amounts of oxomalonic acid (isolated as the sodium salt) are obtained by the action of nitric acid on

sucrose under carefully controlled conditions. CHATTAWAY and HARRIS, J. Chem. Soc. **121**, 2704 (1922).

(*b*) When dihydroxyacetone is heated in aqueous solution with cupric acetate, the product is chiefly oxomalonic acid. EVANS and WARING, J. Am. Chem. Soc. **48**, 2680 (1926).

**Glutamic acid** (5, 63):

(*a*) By the hydrolysis of gluten flour with hydrochloric acid and crystallization of the hydrochloride. The free acid is liberated from the hydrochloride by the action of aniline. ANSLOW and KING, Biochem. J. **21**, 1171 (1927).

(*b*) From beet sugar molasses residues. LARROWE CONSTRUCTION Co., Brit. pat. 265,831 (1926). [C. A. **22**, 509 (1928).]

**Glycine** (4, 31):

The preparation of glycine from chloroacetic acid by the action of ammonia has been improved so as to furnish a 63 per cent yield. ROBERTSON, J. Am. Chem. Soc. **49**, 2889 (1927).

**Hydrazine sulfate** (2, 37):

Hypochlorite solution is added, with stirring, to ammonia solution containing gelatin. MAGIDSON and FRENKEL, Trans. Sci. Pharm. Inst. (Moscow) 6, 25 (1923). [C. A. **22**, 3881 (1928).]

**Ketene** (4, 39):

(*a*) Further details are given. HURD and TALLYN, J. Am. Chem. Soc. **47**, 1427 (1925).

(*b*) An apparatus for the preparation of small amounts of ketene from acetone is described. BILTZ, Z. angew. Chem. **36**, 232 (1923).

(*c*) Metallic sulfates are claimed to act as catalysts in the preparation of ketene in over 80 per cent yields from acetone. KETOID Co., Brit. pat. 237,573 (1924). [C. A. **20**, 1415 (1926).]

(*d*) By passing carbon monoxide and hydrogen over granular zinc oxide under pressure at 260–270°. DREYFUS, Brit. pat. 262,364 (1925). [C. A. **21**, 3626 (1927).]

(*e*) In 80 per cent yields by passing acetone vapor through a

copper tube packed with copper or silver turnings (to permit heat interchange) at 650–670°. No catalyst is necessary, but traces of nickel or iron bring about a secondary decomposition which greatly diminishes the yield. CLARKE and WARING, U. S. pat. 1,723,724 (1929). [C. A. **23**, 4485 (1929).]

**Methylamine hydrochloride** (3, 67):

By passing methyl alcohol and ammonia over thoria at 325–330°. DAVIS and ELDERFIELD, J. Am. Chem. Soc. **50**, 1786 (1928).

**Methylene bromide** (9, 56):

(*a*) In 80 per cent yields from bromoform and alkaline potassium arsenite. KOCHESKOV, J. Russ. Phys. Chem. Soc. **60**, 1191 (1928). [C. A. **23**, 2931 (1929).]

(*b*) A discussion of the mechanism of the reduction of bromoform by sodium arsenite. KOZESCHKOW, Ber. **61**, 1659 (1928).

**α-Methyl *d*-glucoside** (6, 64):

By boiling glucose for four and one-half hours with twice its weight of methyl alcohol containing 3 per cent of hydrochloric acid. PATTERSON and ROBERTSON, J. Chem. Soc. **1929**, 300.

**Nicotinic acid** (4, 49):

By oxidizing nicotine with potassium permanganate; purified by subliming in vacuo and crystallizing from water; m.p. when pure, 236–237° (corr.). SPÄTH and SPITZER, Ber. **59**, 1482 (1926).

***m*-Nitrochlorobenzene** (3, 79):

Nitrobenzene can be chlorinated at 40–50° by the use of 1 per cent of iron with 0.1 per cent of iodine as a combined catalyst. FIERZ–DAVID, Naturwiss. **17**, 13 (1929).

**Nitrourea** (5, 85):

A modification of the directions in Organic Syntheses which improves the yield. The amount of sulfuric acid is diminished and a method of recrystallization is given. DAVIS and BLANCHARD, J. Am. Chem. Soc. **51**, 1794 (1929).

**Pentaerythritol** (4, 53):

Essentially the process described in Organic Syntheses. AARONSON, U. S. pat. 1,678,623 (1928). [C. A. **22**, 3418 (1928).]

**Pentene-2** (7, 76):

By reduction of the corresponding acetylene with hydrogen and colloidal palladium. BOURGUEL, Bull. soc. chim. **41**, 1475 (1927).

**Phenylhydrazine** (2, 71):

By reduction of benzenediazosulfonate with sulfur dioxide. PUTOKHIN, Trans. Inst. Pure Chem. Reagents (Moscow) **1927**, 70. [C. A. **22**, 1337 (1928).]

**$\beta$-Phenylhydroxylamine** (4, 57):

(*a*) In 80 per cent yield by the action of ethereal hydrogen peroxide on $C_6H_5NHMgBr$ at $-25°$. DURAND and NAVES, Compt. rend. **180**, 521 (1925); ODDO and BINAGHI, Atti accad. Lincei **32**, II, 349 (1923); Gazz. chim. ital. **54**, 193 (1924). [C. A. **18**, 3166 (1924).]

(*b*) By the reduction of nitrobenzene with sodium in liquid ammonia. WHITE and KNIGHT, J. Am. Chem. Soc. **45**, 1784 (1923).

***n*-Propylbenzene** (4, 59):

(*a*) By the action of ethyl *p*-toluenesulfonate on benzylmagnesium chloride. GILMAN and BEABER, J. Am. Chem. Soc. **47**, 523 (1925).

(*b*) Benzylmagnesium chloride is treated with $\beta$-chloroethyl *p*-toluenesulfonate, and the resulting $\gamma$-chloropropylbenzene is reduced by treating its Grignard reagent with water. BERT, Compt. rend. **186**, 373 (1928).

(*c*) By the action of ethylmagnesium bromide on benzyl chloride in boiling ligroin (70–90°) solution. BERT, Compt. rend. **186**, 587 (1928).

**Pyrrole** (9, 78):

Ammonium mucate is heated with an equal weight of glycerol; yields of 40 52 per cent of the theoretical amount are

obtained. The presence of an excess of ammonia is of no advantage. BLICKE and POWERS, Ind. Eng. Chem. **19**, 1334 (1927).

**Pyruvic acid** (4, 63):

The ethyl ester is prepared in 60 per cent yield by passing ethyl lactate with air or oxygen over a vanadium pentoxide catalyst. BOEHRINGER SOHN, U. S. pat. 1,614,195 (1927). [C. A. **21**, 746 (1927).]

**Quinoline** (2, 79):

The violence of the original Skraup procedure may be eliminated by the addition of 100 cc. of 80 per cent acetic acid for every 60 cc. of 95 per cent sulfuric acid. COHN and GUSTAVSON, J. Am. Chem. Soc. **50**, 2709 (1928).

***o*-Tolunitrile and *p*-tolunitrile** (4, 69):

(*a*) The process described in Organic Syntheses. CLARKE and READ, J. Am. Chem. Soc. **46**, 1001 (1924).

(*b*) Nickel cyanide is said to be better than copper cyanide in the preparation of nitriles by the Sandmeyer reaction. KORCZYNSKI and FANDRICH, Compt. rend. **183**, 421 (1926).

**Tricarballylic acid** (4, 77):

By heating propane-$\alpha,\beta,\beta,\gamma$-tetracarboxylic acid, and by hydrolysis of the ester of this acid. PERKIN and PINK, J. Chem. Soc. **127**, 191 (1925); GAULT and KLEES, Bull. soc. chim. (4) **39**, 892 (1926).

# ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers in parentheses following the name of a compound, refer to a number and page of Organic Syntheses.)

**Adipic acid** (9, 90): For 62,919 read 62,831.

**Benzalacetone** (3, 17). Following the directions, but replacing the benzaldehyde by an equivalent quantity (540 g.) of anisaldehyde, anisalacetone (b.p. 180–185°/18 mm., m.p. 72–74°) has been obtained in a yield of 83 per cent of the theoretical amount. The distillation residue, on recrystallization from ethyl acetate, yields 18 g. of dianisalacetone (m.p. 128–129°).

**Ethyl cyanoacetate** (9, 91). For Urushibana read Urushibara.

**Nitromethane** (9, 92). For Carcarras read Carcanas.

# SUBJECT INDEX

(This Index Comprises Material from Volume X Only.)

(Names in capital letters refer to titles of individual preparations. Numbers in italics refer to preparative directions for substances formed either as principal products or as by-products; numbers in ordinary type indicate pages on which compounds or subjects are mentioned in connection with other preparations. For example: BROMOACETONE, 1, *12* indicates that bromoacetone is mentioned on page 1 and that directions for its preparation are given in detail on page 12.)